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NUTRITIONAL REQUIREMENTS IN TIME OF WAR*

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WITH many foods in short supply, rationing — some prefer to call it enforced food sharing — is being undertaken. Without a rationing program the only people to get enough would be the ones who have the time to raid the stores when fresh supplies come in. Any course other than rationing would lead to queues and chaos. Failure to control the use of food supplies would make impossible the shipment of food to strengthen our allies, or even to provide what is needed by the United States armies in this country and all around the globe.

There simply is not enough to give everyone all the food he wants to buy. Yet the general food position in this country is not too bad — not now, at any rate. It may be worse before the year is out. If production goals are not attained we shall soon be scraping the bottom of many a barrel. If the machinery for distribution fails to function, we shall undoubtedly be in serious trouble. And we must brace ourselves against possible sudden and unpredictable demands for food that may arise out of opportunities for new invasions, out of unexpected needs on the part of our allies or out of the necessity of providing food to starving people in reoccupied territory, to secure their help in speeding the victory against our common enemies.

However, the food position, I repeat, is now not too bad, and with reasonable good fortune in production, reasonably good management and reasonable willingness on the part of most of us to adjust consumption habits, we the people of this country will undergo only bearable hardships, even allowing for increased military needs.

Government purchases of food to feed our military forces and to help sustain the fighting strength of our allies will amount this year to roughly 25 per cent of the total production of food in this country. Production, however, has increased enough so that despite this requisition of many million tons of food, as much is being left for home consumption as was used in the years before the war. Some commodities, including milk and poultry, are in larger supply than they were then; others, notably butter and commercially processed fruits, are shorter in supply. The figure for red meat — strange as this may sound to the many who have almost forgotten the aroma of a well-cooked beefsteak — is almost the same as that for the period 1935–1939: 124.5 pounds per capita per annum now, 126.3 pounds then. Also, the average diet, judged in terms of the nutrients provided per capita per day, is essentially the same. Were the foods distributed with perfect equity — to each according to his needs — the calories, protein, minerals and vitamins provided would fully meet for everyone the recommendations of the Food and Nutrition Board of the Division of Biology and Agriculture, National Research Council, with something of every nutrient to spare.

Perfect equity of distribution, however, is not to be expected under any system and was not attained at any time before the war. In 1935–1936 some 35 per cent of the families whose purchases of food were studied by the Bureau of Home Economics had diets that were rated as less than fair, and were the recommended daily allowances of the National Research Council to be applied as the yardstick, this percentage would be much greater. There are at least three explanations for the defective diets in 1935–1936. First, a bad nutritional environment was in part responsible. Many foods as purchased were impoverished by methods of processing, notably products derived from bread grains and some processed fruits and vegetables. Furthermore, the consumption of sugar was excessive. In such an environment it is difficult to choose a good diet without more knowledge of nutrition than most persons have. Secondly, lack by the large majority of the population of the most elementary

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knowledge of how to select a good diet must have contributed to many defective diets. Lastly, the food supplies available, owing largely to the low purchasing power of a high percentage of the population, were unequally distributed.

The less expensive foods are in general more impoverished by processing than are other foods. The so-called "protective foods" like milk, meat and fresh vegetables and fruits are usually higher priced. With the better money wages earned by many persons in 1942, consumption of the more expensive protective foods was greatly increased. Yet even in that year of luxury consumption (1942), analyses of family food expenditures, based on a survey of family spending and saving in wartime as published by the Office of Price Administration, revealed that at least 20 per cent of the population were not receiving annual incomes large enough to purchase the food necessary for a good diet.

It has been stated above that the provision of nutrients per capita per day obtained from the total supplies of food available for consumption by civilians in 1943 compares favorably with that for the period 1935–1939. For a large proportion of the population the nutritional situation may actually be superior. Factors that may be expected to exert a favorable influence on the position are as follows:

First, methods have been introduced for improving the nutritive quality of several important staple commodities. Chief of these is the enrichment of flour and bread with vitamins and iron. It is estimated by the milling industry that 80 per cent of the white flour is now enriched with thiamine and niacin. An order of the Food Distribution Administration requires enrichment of all white baker's bread, and approximately 90 per cent of the margarine produced is now fortified with vitamin A. Because of the fact that the cheaper commodities contribute relatively more calories to the diets of persons in low-income groups, the restorative fortifications of flour, bread and margarine that were recommended by the Food and Nutrition Board of the National Research Council have effected a wider distribution of the vitamins and minerals involved. The curtailment of supplies of sugar to approximately 70 per cent of prewar consumption is also beneficial.

Secondly, an intensive campaign of education in nutrition has been under way since the National Nutrition Conference was held in Washington in May, 1941. This campaign, directed and coordinated by the Nutrition Division, formerly in the Office of Defense Health and Welfare Services but now a part of the Food Distribution Administration, has extended into almost every hamlet in this country. It has probably not reached down into the lower levels of literacy. Nevertheless, its effects are making themselves apparent in many homes through the selection of better foods and diets.

Thirdly, increased employment and increased incomes for large sections of the population have resulted in consumption of more of the protective foods — milk, meat, vegetables, fruits and so forth — by many persons who previously could not afford these foods. One effect of this has been to create shortages, notably of meat and butter. This experience has demonstrated for all time that the supposed surpluses of foods in the years before the war were not surpluses at all but relative deficits that were masked by inequality of distribution.

Lastly, rationing of processed fruits and vegetables and of meats, fats and cheese should have the effect of diminishing waste of food, and thus lead in turn to more effective use of the food supplies available.

Factors the effect of which may be unfavorable for the food position, especially for that section of the population with low fixed incomes, are as follows: the relatively higher cost of many foods; the abandonment or limitation of direct distribution of food and the food-stamp plan; and difficulties attending the transition to controlled distribution procedure, together with associated "black markets" and discrimination on the part of legitimate distributors in favor of former and nearby customers. Lack of satisfactory machinery for obtaining information on consumption makes it impossible to judge the net result of these opposing factors. The importance of securing current surveys of consumption in different areas by geographic position, type of employment and income level is the subject of much discussion at the present time.

Precise evaluation of the amount of poor health attributable to bad nutrition is difficult to obtain, for reasons given in a report of a special committee of the Food and Nutrition Board.[1] What evidence existed up to 1941 pointed to less than satisfactory nutrition in a large segment of every population group that had been studied.

The average American diet has been steadily improving in many ways, although not in all respects, since the last war. This improvement is believed to be a major reason for the increased height and weight of children and soldiers. The average height of the Army inductees is reported as 1 inch greater than the average for United States soldiers in World War I. On the other hand, the proportion of men currently rejected on grounds of physical disabilities has been very large. What proportion of these rejections should be attributed to malnutrition is conjectural. In

my opinion, it is high. Besides the desired surveys on food consumption, there is need for the systematic current application of several clinical tests to groups of the population to obtain a periodic appraisal of the nutritive status of the Nation.

The staff of the Civilian Food Requirements Branch of the Food Distribution Administration is responsible for watching the food position from the standpoint of civilian needs. A representative maintains close contact with each of the several commodity branches of the Food Distribution Administration so that information concerning the supply position of every food commodity is regularly available. At quarterly intervals, or more frequently, an allocation board headed by the director of the Food Distribution Administration reviews the claims for food submitted by the Army, the Navy, the Civilian Food Requirements Branch, the Office of Lend-Lease Administration and other agencies. The decisions concerning allocations are based on the recommendations of this board. Mr. Hendrikson, director of the Food Distribution Administration, takes this position:

> We want our own soldiers to have all the food they need, when they need it, and where they need it. We want to go just as far as we can in meeting the food requirements of our allies. But we also want to — and must — provide American civilians with the food required to do a good job on the home front. The principle that must guide and is guiding the division among these major claimants is this: "How will it help to win the war?" *Viewed in this light, the claims of all are well supported.*

The civilian requirement for each commodity depends on estimates of the physiologic needs of the population as a whole, with due regard to special needs and the requirements of industry and institutions; estimates of past consumption; and judgments concerning the physiologic effects of imposed restrictions on consumption. The estimation of physiologic needs involves continuous reviewing of the entire food position. We can, for instance, do with less red meat, than the present estimated supply of 2 pounds per capita per week if poultry, eggs, dairy products and fish are in adequate supply, but when they in turn are scarce, the requirement for meat becomes more pressing. The same applies to other groups of foods. The essential consideration, from the standpoint of needs, is not the food itself but the nutrients that the food provides — the calories, protein, minerals and vitamins. However, as shortages develop in commodities now unrationed, — and presumably they will, — the necessity for withholding enough of the more essential foods to meet civilian needs will become increasingly more pressing. Furthermore, as other shortages appear the foods involved must be added to the list of rationed foods. To arrange for rationing with the Rationing Division of the Office of Price Administration when shortages develop is also a responsibility of the Civilian Food Requirements Branch.

No system of rationing can be adjusted to satisfy perfectly the real or imagined special needs of everyone. Such a program would break down out of sheer complexity. Differential rationing has been avoided in so far as possible in every country where rationing has been tried except in Germany and Russia. Some degree of differential rationing, however, will undoubtedly be necessary for some commodities, and notably for milk. It is everywhere agreed that the need for milk is greatest in infancy and childhood, in pregnancy and lactation and in sickness. Children, pregnant and lactating women and invalids must have priority on milk even if the rest of the people go without.

This brings me to a subject in which we as physicians are professionally concerned. That is the dietary needs of invalids and hospitals. A division of the Civilian Food Requirements Branch is exclusively concerned with the problems presented by these needs. It is headed by Dr. Fred L. Adair, past chairman of the Department of Obstetrics of the University of Chicago. It has two sections. One deals with the dietary requirements of invalids and hospitals. This section will soon have the direction of a physician with experience in hospital management, who will be aided by expert dietitians. The other section deals with the requirements of pregnancy and childhood. It has been headed for some time by Dr. Sarah Deitrick, of the Children's Bureau.

The ration orders issued up to now permit wide discretion by the local rationing boards in providing supplementary rationed foods for invalids and hospitals. The door was left wide open, — although everyone has not yet discovered it, — but the time will assuredly come when abuses will necessitate correction of this situation. When this occurs, my office and the Food Rationing Division of the Office of Price Administration will want the most authoritative advice obtainable.

For this purpose the National Research Council, at the request of the director of the Food Distribution Administration, has appointed a group of eminent physicians who between them represent in an official capacity several of the professional sections of the American Medical Association; the American Diabetic Association is also represented by one of its officers. The group is called the Subcommittee on Medical Food Requirements. It is organized as a subdivision of the Committee on Drugs and Medical Supplies of the National Research Council. It will develop a procedure for

securing certification by physicians of invalids requiring supplemental rationed foods. This will involve decisions concerning qualifications of medical attendants who may sign certificates for supplemental quantities of rationed foods. It will require a listing of diseases justifying extra allowances of rationed foods, with specific determinations of what foods and what quantity of each should be allowed in cases of each disease; also, a listing of diseases for which certification for supplemental quantities of rationed foods should not be honored. In addition, the Subcommittee on Medical Food Requirements or related regional committees guided by it will receive and act on appeals from decisions of local rationing boards submitted by hospitals or physicians.

It remains to be seen how firm this group must be. The degree of firmness will depend on the tightness of the food position. I can assure you that rationing is not indulged in for the pleasure of rationing, as some critics of the Government have supposed. A comparable body appointed by the Medical Research Council to advise the British Ministry of Foods has been extremely firm. They recognize very few diseases among conditions requiring supplementary quantities of rationed foods. Milk is generously supplied, and a supplemental allowance of meat is allowed for some diseases. The meat ration for hospitals, however, is not increased — on the assumption that many inmates of hospitals eat little or no meat, so that their portions become available for serving other patients who require more than is permitted by the ration.

It may take some months before all this machinery is running smoothly. The greater area and population of this country and the less homogeneous eating habits make the successful application of rationing programs much more difficult here than in Great Britain. In the meantime, some genuine hardships will inevitably develop. They can be corrected. It is to be hoped, however, and I think expected, that nearly everyone will understand that this war can be lost unless the use of food is firmly controlled.

Many adjustments will be necessary, and if the war continues long, food habits will probably undergo great changes. Unless, however, the picture in this country grows much darker than now seems likely, there should be no more malnutrition than there was before the war; indeed, more equitable distribution of food may result in better average health. Success depends on everyone's cooperating to the best of his or her ability. We must see this business through as the British have, with a minimum of actual hardship, a minimum of friction and a maximum of good will.

Reference

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SARCOIDOSIS*

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SARCOIDOSIS, or benign lymphogranuloma, is now recognized to be a generalized disease that may involve any organ in the body, thereby giving rise to many clinical syndromes. When first described by Hutchinson[1] in 1875, however, it was thought to be a disease of the skin characterized by granulomatous infiltration. Fourteen years later, Besnier[2] described similar lesions involving the nose, ears and fingers in particular and termed the condition "lupus pernio." In 1899, Boeck[3] studied these lesions histologically and recorded in addition that the mucous membranes and lymph nodes are not uncommonly involved in the process. He attached the name "sarcoid" to the disease. It was not until 1914, when Schaumann[4] demonstrated that the tonsils, bones, lungs and internal organs may be involved, that the systemic nature of sarcoidosis was recognized. Kuznitsky and Bittorf[5] the following year again emphasized that the cutaneous manifestations are a part of a diffuse granulomatous systemic disease. These two observers stressed the importance of the pulmonary lesions in particular. Jungling[6] in 1919 called attention to the bone changes. In 1909, Heerfordt,[7] an ophthalmologist, described the syndrome consisting of ocular lesions and parotitis with bilateral facial paralysis. The relation between this uveoparotid syndrome and the skin lesions of sarcoidosis was recognized by Pautrier[8] in 1938.

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Etiology

The cause of sarcoidosis is not clear. Many pathologists believe that it is a benign form of tuberculosis, basing this concept on the histologic similarity between the two conditions, the occasional

recovery of tubercle bacilli and the reported cases of termination in frank tuberculosis. Against this concept are the facts that tubercle bacilli usually cannot be demonstrated by culture or animal inoculation and that 60 to 80 per cent of cases fail to show positive skin reactions to tuberculin. The proponents of the theory explain this by an atypical or nonacid-fast phase of the bacillus. Schaumann[4] cultivated from the lesions a group of pleomorphic organisms that he believed to represent such a phase, and they have been observed to become acid fast on passage. Several other reports[9, 12] give further support to the theory that sarcoidosis is due to an atypical tubercle bacillus and that its peculiar manifestations are due to lack of tuberculin allergy. In these cases the administration of B.C.G. to patients with sarcoidosis failed to produce tuberculin sensitivity.

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According to Filho,[13] the entire sarcoid syndrome may be found in leprosy, including skin lesions, bone changes, lymphadenopathy and anergy to tuberculin. Longcope and Pierson[14] were unsuccessful in their attempt to grow fungi from the lesions.

Williams and Nickerson[15] prepared from proved skin lesions an antigen that they injected intradermally into patients suspected of having sarcoidosis. In 4 cases, an erythematous reaction appeared in twenty-four hours. Such a reaction may be nonspecific, however, and Harrell[9] was unable to duplicate these results using an extract prepared from lymph nodes. The presence of eosinophils in the blood stream in some cases suggests an allergic state. The fact that neutropenia and leukopenia may be found in the disease suggests that a virus is the etiologic agent. Harrell thinks that these patients exhibit an exaggerated nonspecific response to small amounts of a lipid fraction of a single organism or a variety of organisms. This response is analogous to the necrosis, infiltration by polymorphonuclear neutrophils and edema of the familiar allergic reaction to proteins. At the present time, however, on the basis of existing evidence, the etiology is obscure.

Pathology

The pathologic picture is characteristic, and no matter what structures are involved, the lesions are identical. The typical lesion is about the size of a miliary tubercle and is composed of large, pale-staining, polygonal epithelioid cells. Small lymphocytes may be found scattered among these cells. Between nodules there is little fibrosis, but in lesions of long duration the connective tissue may be hyalinized and the reaction to Congo red stains for amyloid on this type of tissue is occasionally positive.[9] There is no peripheral inflammatory zone about the nodules, and caseation is absent. Although necrosis is not a frequent finding, small areas are occasionally seen in the central cells. Giant cells are noted at times, but are rarely numerous. When present, they are very large, with as many as twenty pale nuclei, and contain peculiar inclusions that stain intensely with hematoxylin. Giant cells occur with special frequency in the presence of degeneration of the central cells.

The solitary tuberclelike lesions do not grow in size, but increase in number, at times so much so that they form shiny, pearly-gray masses that are plainly visible to the naked eye and give the appearance of tumors in the skin or masses in the spleen, liver, heart or other organs. When the lesions regress, there is a tendency to fibrosis and hyalinization. The skin, lymph nodes, lungs, bones, liver and spleen are most commonly involved, but no organ in the body is exempt. Schaumann[4] emphasized the frequency with which lymphoid tissue is affected.

Clinical Data

Clinically, sarcoidosis is characterized by widespread involvement of one or more organs, with few constitutional manifestations. Many investigators have reported that the disease occurs most often among Negroes, Puerto Ricans and Indians; whereas according to others there is no special race incidence. The disease begins insidiously in early adult life or childhood and usually pursues an indolent course. The diversity of its clinical forms is explained by the association of lesions in multiple organs. Contrariwise, seldom are all the organs involved in the same patient. Although skin lesions are frequent, the disease may be widely disseminated in their absence. The skin lesions are of several types; painless, nonpruritic, violaceous plaques with no surrounding erythema or induration, occurring most frequently on the face, arms and legs, but at times widespread; localized nodular lesions, most commonly involving the eyelids, nares, fingers and ears; and combinations of these two. Destruction and distortion of the nares may occur. The nails may be striated and brittle, and the nail beds often show the lesions. The oral and nasal mucosa may be involved.

The commonest initial finding in sarcoidosis is enlargement of the superficial lymph nodes. The adenopathy may be limited or generalized, and varies considerably in degree. The nodes are firm, rubbery, discrete and usually painless and do not adhere to surrounding tissues. The nodes most frequently involved are the preauricular, postauricular, submaxillary, submental and epitrochlear. Lymph nodes along the course of the major lymphatic vessels in the arm may be palpable, and those of normal size or only slightly enlarged may show a typical sarcoid lesion.

Pulmonary lesions are common, and several types have been described. Marked bilateral, symmetrical enlargement of the hilar and peribronchial lymph nodes is commonly the only pulmonary manifestation. In other cases, dense radiations extend from the enlarged hilar nodes into the lung fields, most often along the medial portions of the lower lobes. A frequent type is a nodular infiltration distributed bilaterally, granular in appearance and resembling miliary tuberculosis. A soft infiltration resembling caseous pneumonic tuberculosis is found at times. Honeycombing and larger cavity formations may be present. Enlargement of the lymph nodes in the superior mediastinum, especially on the right, may accompany the pulmonary lesions. X-ray films of the chest are not a guide to the severity of the disease,[16] since extensive pulmonary infiltrations may be accompanied by little evidence of a disseminated process, and may resolve completely, whereas slight pulmonary involvement may be associated with extensive lesions in other organs, resulting in serious disability. There is a tendency for the pulmonary lesions to clear completely or almost completely. In a series of cases cited by King,[16] resolution occurred in 60 per cent in seven weeks to three years, with an average of twenty-two months. A return of pulmonary lesions is unusual after clearing has occurred. There is some disagreement whether fibrosis may result from the healing of lesions in the lungs.

Bone lesions occur in 10 to 20 per cent of cases, usually involving the phalanges, metacarpals and metatarsals. The tarsal and carpal bones and occasionally the long bones may, however, be affected. Circumscribed cysts without change in the density of the surrounding bone represent the usual type of involvement. In other cases the bone has a latticework or reticulated appearance, with thickened trabeculae contrasting with rarefaction in the rest of the bone. The periosteum and joints are not involved. The lesions are chronic, and may resolve or progress irregularly. They do not perforate and form fistulas, but there may be inflammation and tenderness of the overlying tissues.[17] Deformities and even painless mutilation of the fingers such as occur in leprosy are seen. X-ray examination of the bones is rarely positive in the absence of some obvious deformity.

Any of the structures of the eye may be involved. Conjunctivitis, keratitis, iridocyclitis or more extensive uveitis may occur. The lesions in the cornea, iris or uveal tract may heal and leave scars and synechiae. The eye involvement is most often mistaken for syphilis or tuberculosis. In some cases the parotid gland may be affected along with the eye, giving rise to the syndrome formerly called uveoparotid fever. The other salivary glands, or the lachrymal and mammary glands may be the seat of sarcoidosis. Involvement of muscle, peripheral nerves and the central nervous system has been noted.

Little attention has been paid to the important effects that sarcoidosis produces on the heart. Salvesen[18] first recorded a case of myocardial involvement resulting in bundle-branch block. Schaumann[19] observed that at times heart failure results. Longcope and Fisher[19] report 5 cases of sarcoidosis that showed evidence of myocardial insufficiency during life. Heart failure, arrhythmias or significant electrocardiographic changes are reported in these patients. Invasion of the pericardium by sarcoid may also occur. Cardiac function may be secondarily affected as a result of extensive pulmonary involvement, with resultant strain on the right ventricle or even right-sided heart failure.

Localization in the liver, spleen, stomach, intestines, kidney and epididymis occurs. Rotenberg and Guggenheim[20] report a case of sarcoidosis in which renal insufficiency and hypertension may have been due to sarcoid invasion of the kidneys.

Cases with involvement of the pituitary gland have been reported. Diabetes insipidus was present in most of them. A case of insufficiency of the anterior lobe of the pituitary gland due to sarcoid infiltration has recently been reported.[21]

Owing to the fact that groups of organs may be involved in almost innumerable combinations, a great variety of clinical syndromes result. It is to be noted, however, that all the extracutaneous lesions are characterized by their latency and their tendency to spontaneous regression, in contrast to the much more chronic behavior of the skin lesions.

It has already been mentioned that sarcoidosis is accompanied by few constitutional symptoms. Occasionally weakness, fatigability, anorexia, weight loss or arthralgia occurs. These symptoms, however, are rarely prominent. Fever may be present, usually in association with uveoparotiditis or acute progressive phases of the disease. Longcope[22] emphasizes that symptoms are caused by "mechanical interference with the function of organs rather than by any form of intoxication." The sarcoid lesions by exerting pressure on normal tissue displace or destroy it. When the lesions are in the skin or superficial lymph nodes, symptoms are lacking. The opposite is true, however, when the eye, mediastinum, heart, lungs, central nervous system or other important organs are the seat of sarcoid tumorlike masses. A puzzling feature of sarcoidosis of the lung is the paucity of symptoms and signs in the presence of extensive pulmonary involvement. However, dyspnea, cough and transient chest pain may be present. Hemoptysis occurs

but is rare.[23] Secondary infection resulting in bronchopneumonia is not uncommon. Tuberculosis often develops in cases of pulmonary sarcoidosis.

Laboratory Data

The laboratory findings, though not constant, may be of aid in supporting the diagnosis. Anemia is not often present. The white-cell count is usually normal or below normal. Marked leukopenia suggests splenic involvement, whether or not the spleen is palpably enlarged. The only abnormality of any significance in the differential count is eosinophilia. Some cases, however, never have eosinophilia, whereas in others it is transient. Some observers consider eosinophilia an index of activity. Harrell[9] observed that showers of large mononuclear cells were present if differential counts were often repeated. The rise occurs at the expense of the polymorphonuclear leukocytes. The sedimentation rate is usually elevated during the active stage of the disease. Since, however, hyperglobulinemia may be present, the sedimentation rate cannot be used to indicate activity, for hyperglobulinemia increases the rate.[24]

Harrell and Fisher[25] have discussed the changes in blood chemistry. They found the blood calcium to be normal or above normal and the serum phosphatase usually increased in the active phase. The latter finding could not be correlated with the duration of the illness or the site or extent of the lesions. Nonprotein nitrogen and phosphorus levels are normal. The total cholesterol is low or normal. The plasma proteins show an interesting variation. The globulin fraction is commonly elevated sufficiently to raise the total plasma protein. When the total proteins are within normal limits, the globulin fraction is often larger than normal and in excess of the albumin fraction. The plasma albumin is normal or slightly decreased. The urine is usually normal, although Harrell[9] in 2 cases found a substance resembling Bence-Jones protein in its solubility at the boiling point.

Course of Disease

Sarcoidosis is characterized by a chronic, usually benign course and periods of remission. Complete cure may occur. The two shortest reported periods of recovery are five and twenty-seven months. Recovery may be spontaneous, or simultaneous with the development of intercurrent tuberculosis. The prognosis is good, and the disease is usually not fatal except when vital organs are involved.

Diagnosis

Sarcoidosis must be differentiated from Hodgkin's disease, lymphosarcoma, bronchiolitis fibrosa obliterans, erythema nodosum, leukemia, fungous infection, tuberculosis, especially the noncaseous variety, and syphilis. The correct diagnosis is usually made by exclusion or biopsy. When enlargement of lymph nodes predominates, the disease must be differentiated from follicular lymphoblastoma (giant lymph-follicle hyperplasia).[26] This is a relatively benign disease of the lymphatic system characterized by lymphadenopathy (due to dimensional and numerical hyperplasia of the follicles), splenomegaly (60 per cent of cases), a normal blood picture, absence of cachexia, a long course and a prompt response of the lymph nodes and spleen to x-ray therapy in the early stages of the disease. The pathologic picture is characteristic.

Treatment

Various types of treatment have been advocated. Arsenicals, iodides, leprosol, tuberculin, hyperpyrexia, gold salts, roentgen rays[27] and radium have been used without great success. Carbon dioxide snow and x-ray therapy have, however, been of some value in the treatment of skin lesions. Longcope[22] has observed a favorable effect of ultraviolet irradiation on the skin lesions and superficial lymph-node enlargement. Others have noted no benefit from its use. As a matter of fact, it is difficult to evaluate any form of therapy in view of the natural tendency of the disease to undergo spontaneous remission. Until more is known of the etiology and pathogenesis of sarcoidosis, treatment must remain empirical.

Case Reports

Case 1. A 19-year-old Negress developed a mild upper respiratory infection. For the ensuing 2 weeks, she had moderate weakness, nonproductive cough and considerable dyspnea even while at rest. X-ray examination of the chest led to a diagnosis of pulmonary tuberculosis and the patient was sent to a sanatorium. While there, she continued to be weak and dyspneic. Examination of the sputum was repeatedly negative for tubercle bacilli and fungi. Intradermal tuberculin tests with P.P.D. (purified protein derivative), first and second strengths, were negative. A splenic puncture was negative. After 1½ months, the patient was transferred to the Gallinger Municipal Hospital for further studies.

Her past history disclosed that she had been frail and short of breath for as long as she could remember. As a child, she had been unable to play with other children because of dyspnea.

At the time of admission to the hospital, the patient appeared asthenic. While she was lying flat in bed, the breathing was rapid and shallow. The temperature was 98°F., the pulse 80 and regular, and the respirations 36. A firm movable lymph node 1.5 cm. in diameter was felt 7 cm. above the middle third of the right clavicle. The heart was normal. Subcrepitant rales were heard over the upper halves of both lungs, and there was bronchial breathing over the upper portion of the right and left lower lobes and over the right middle lobe. The

spleen was felt one fingerbreadth below the costal margin and was firm and smooth.

An x-ray film of the chest (Fig. 1) showed diffuse infiltration and mottling throughout both lungs. In the

FIGURE 1. *Case 1.*
Note the diffuse infiltration and mottling with small areas of cavitation in the upper lobes and prominent hilar shadows.

upper lobes there were small areas of cavitation. The hilar shadows were prominent. Films of the hands and feet were negative. The red-cell count was 5,530,000, and the white-cell count 5800, with 64 per cent neutrophils, 30 per cent lymphocytes and 6 per cent monocytes. The serum albumin was 3.39 gm., and the serum globulin 3.02 gm. per 100 cc. Urinalysis was negative. Biopsy of the cervical lymph node resulted in a diagnosis of sarcoidosis.

The patient's course was uneventful until the 17th hospital day, when she suddenly became orthopneic and cyanotic. The temperature rose to 103°F. and the pulse to 150. On the following day, the liver was tender and extended four fingerbreadths below the costal margin. The venous pressure was 220 mm. of saline solution and rose to 270 mm. on pressure in the right upper quadrant. The arm-to-tongue circulation time, measured with 10 per cent magnesium sulfate, was 31 seconds. The dyspnea and cyanosis continued and the patient died on the 18th hospital day.

Autopsy. The right ventricle of the heart was hypertrophied and dilated. The right auricle was dilated. There was no evidence of sarcoid involvement of the myocardium. The pericardium was normal. Both lungs were studded with grayish masses. On sectioning the lung, these masses were not necrotic and at the apices small cavities with smooth walls were seen. There was no evidence of caseation. The microscopic sections showed typical sarcoid lesions. Occasional giant cells were seen in these sections. The spleen weighed 550 gm. and contained numerous large gray masses 1 to 3 cm. in diameter. Microscopic examination showed evidence of sarcoidosis. The liver weighed 1700 gm. Small gray masses about 0.5 cm. in diameter were seen on the surface and on a cut section. The lesions of sarcoidosis were seen on microscopic examination. The pancreas, adrenals and gastrointestinal and genitourinary tracts were normal.

Comment. This case represents sarcoidosis involving several organs. The clinical and pathological findings suggested chronic strain of the right ventricle due to severe pulmonary disease, and the immediate cause of death was acute failure of the right ventricle.

CASE 2. A 22-year-old Negro developed a mild, nonproductive cough and dyspnea on exertion 3 weeks before admission. On the advice of his physician, an x-ray film of the chest was taken, and on the strength of this the patient was referred to the hospital with a diagnosis of far-advanced pulmonary tuberculosis. The past history was negative except for a corneal ulcer at the age of 10.

At physical examination the patient looked well developed, well nourished and healthy. The only positive

FIGURE 2. *Case 2.*
Note the bilateral enlargement of the hilar nodes and diffuse mottled infiltration throughout both lungs.

findings were a right corneal scar 0.3 cm. long, bilaterally palpable epitrochlear lymph nodes 1 cm. in diameter and occasional sibilant rales in the right hemithorax.

The red-cell count was 4,900,000, and the white-cell count 4000, with 57 per cent neutrophils, 39 per cent lymphocytes, 3 per cent monocytes and 1 per cent eosinophils. Examinations of six sputums and one gastric washing were negative for tubercle bacilli. The intradermal tuberculin test with P.P.D., first strength, was negative, but the test was slightly positive with P.P.D., second strength. The serum calcium was 12 mg. per 100 cc., the serum albumin 5.27 gm., and the serum globulin 3.35 gm. An x-ray film of the chest (Fig. 2) showed bilateral enlargement of the hilar lymph nodes and a diffuse, mottled infiltration throughout both lungs.

Biopsy of an epitrochlear lymph node revealed findings typical of sarcoidosis.

As the patient felt well, he was discharged to return each month for a check-up examination.

Comment. This case is quite typical of sarcoidosis with diffuse pulmonary involvement, few symptoms and no constitutional reaction. The corneal ulcer at the age of 10 may have been due to sarcoidosis.

Case 3. A 42-year-old Negress was admitted to the hospital complaining of cough and fever. Ten days previously, she had a severe chill followed by fever. For the ensuing 10 days, she remained in bed because of weakness, dyspnea and a severe, dry cough. There were no chest pains, hemoptysis or night sweats.

Figure 3. *Case 3.*
Note the diffuse infiltration and cavity formation, most marked in the upper halves of both lungs.

The past history revealed that the patient had been short of breath for 1 year. The dyspnea had become progressively but only slightly worse until the onset of the present illness, when it became so severe that the patient could not lie flat in bed. Six years before admission, a nodular rash had appeared on the cheeks and nose. A biopsy of the skin taken at the Dermatology Clinic of the Georgetown Hospital had established the diagnosis of sarcoid.

At physical examination the patient looked seriously ill. The temperature was 102.5°F., the pulse 120, and respirations 40. On both cheeks and spreading across the bridge of the nose was a dark-red nodular lesion. The nares were enlarged and distorted. A similar lesion was present on the right upper eyelid, the right side of the lower jaw and the right elbow. Several submaxillary lymph nodes were enlarged, firm and freely movable. The right index finger and the left ring finger were broader than the others. The distal phalanges and nails of these fingers were deformed. There was slight dullness over both upper lobes anteriorly. Over the right hemithorax and left upper lobe, sibilant and sonorous rales were heard. Bronchial breathing and subcrepitant rales were present over the right upper lobe. At both bases subcrepitant rales were heard.

The red-cell count was 3,500,000, and the white-cell count 7000, with 58 per cent neutrophils, 23 per cent band forms, 12 per cent monocytes, 6 per cent lymphocytes and 1 per cent eosinophils. Urinalysis was negative. The serum albumin was 2.17 gm., and the serum globulin 4.76 gm. per 100 cc. Intradermal tuberculin tests with P.P.D., first and second strengths, were negative. The sputum was negative for tubercle bacilli on six occasions. An x-ray film of the chest (Fig. 3) showed diffuse mottling and fibrosis throughout the greater portion of the right lung and the upper half of the left lung. There were many small cavities in the left upper lobe and a large fluid-containing cavity 4 cm. in diameter in the right upper lobe. X-ray films of the hands and feet (Fig. 4) showed many sharply punched-out areas indicating bone resorption in the phalanges of the right index and left ring fingers and in several of the carpal and metacarpal bones. An electrocardiogram showed low T waves in Leads 1 and 4, which were suggestive of myocardial damage.

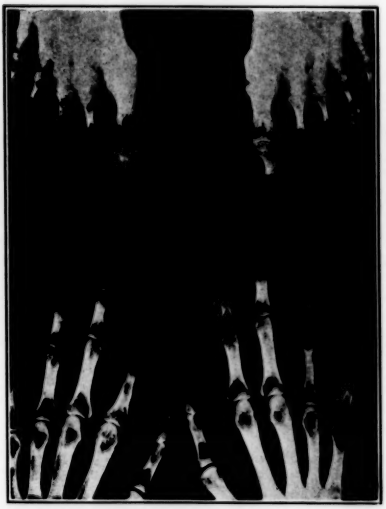

Figure 4. *Case 3.*
Note the many sharply punched-out areas, most marked in the phalanges of the right index and left ring fingers.

The patient was given sulfadiazine. After 4 days, the temperature, pulse and respirations were normal. The chest findings were unchanged, except for the disap-

pearance of the basal rales. Re-examination of the chest by x-ray 10 days after admission showed no appreciable change except that the cavity in the right upper lobe was empty. The temperature remained normal and the patient was symptom free at discharge on the 25th hospital day.

Comment. This is a case of sarcoidosis with skin, bone and pulmonary lesions and a superimposed pneumonia that responded to chemotherapy.

CASE 4. A 46-year-old Negro had transient pain in the left side of the chest in May, 1941. The pain was dull and slightly intensified by deep breathing. A physician sent him to the District of Columbia Chest Clinic, where an x-ray film of the chest was taken. He was then sent to the Glenn Dale Sanatorium.

The past history revealed a loss of 20 pounds during the preceding 5 months. This the patient attributed to hard work as a laborer. He had been in a tuberculosis sanatorium for 5 months in 1931 because of "swollen glands" in his neck. At that time he noticed a skin lesion above the left clavicle.

He remained at the Glenn Dale Sanatorium until November, 1941, and left against advice. While there he gained 17 pounds and was symptom free. All sputum examinations were negative for tubercle bacilli. From November, 1941, until May, 1942, the patient stayed at home and continued to feel perfectly well. During this

FIGURE 5. *Case 4.*

Note the numerous areas of infiltration and honeycombing throughout the greater portion of the left lung and the middle third of the right.

period frequent sputum examinations were negative for tubercle bacilli. In May, 1942, he was advised to enter the Gallinger Municipal Hospital for further study.

At physical examination the patient was slightly obese and appeared to be in excellent health. There were dark-red skin lesions in patches above the left clavicle. The lesions were nonscaly, nonindurated and raised in plaques. There was slight diminution in breath sounds over the left lower lobe. The remainder of the examination was negative.

An x-ray film of the chest (Fig. 5) showed numerous areas of infiltration and honeycombing throughout the greater portion of the left lung and middle third of the right lung. At the left base there was evidence of thickened pleura. X-ray films of the hands and feet were negative. Examinations of the sputum and gastric washings were repeatedly negative for tubercle bacilli. Sputum culture for fungi was negative. An intradermal tuberculin test was positive. The sedimentation rate (Ernstene–Rourke method) was 1.55 mm. per minute (normal, 0.35 mm.). The serum albumin was 2.92 gm., the serum globulin 5.16 gm., and the serum calcium 11.8 mg. per 100 cc. The red-cell count was 4,000,000, and the white-cell count 5600, with 39 per cent neutrophils, 51 per cent lymphocytes, 7 per cent monocytes, 2 per cent eosinophils and 1 per cent basophils. A biopsy of the skin lesion showed sarcoid.

Comment. This is a case of sarcoidosis with skin and pulmonary lesions. The diagnosis was suggested by the evidence of diffuse pulmonary disease resembling tuberculosis in the absence of symptoms and signs of that disease.

CASE 5. A 24-year-old Negro was admitted complaining of swollen femoral and axillary lymph nodes. Ten months previously, he noticed slight, painless swelling of the femoral lymph nodes on both sides. A short time later, he noticed similar swelling of the axillary lymph nodes. These groups of nodes gradually became larger. The bulging of the femoral nodes through his trousers caused him considerable embarrassment, and for this reason he sought admission to the hospital.

At physical examination the patient looked well developed, well nourished and healthy. The preauricular, axillary, cervical, epitrochlear, inguinal and femoral lymph nodes were enlarged. They were discrete, rubbery, movable and nontender. The axillary nodes were about 3 cm. in diameter and the femoral nodes about 6 cm. in diameter. Over both knees and the back of the neck were hard, salmon-colored plaques 0.5 to 1.0 cm. in diameter. The remainder of the examination was negative.

An x-ray film of the chest (Fig. 6) showed bilateral enlargement of the hilar lymph nodes. Films of the hands and feet were negative. The red-cell count was 5,580,000, and the white-cell count 3600, 69 per cent neutrophils, 27 per cent lymphocytes, 3 per cent eosinophils and 1 per cent basophils. Urinalysis was normal. The corrected sedimentation rate (Wintrobe method) was 38 mm. per hour. The serum albumin was 4.85 gm., and the serum globulin 3.96 gm. per 100 cc. Intradermal tuberculin tests (P.P.D., first and second strengths) were negative. A biopsy of a lymph node revealed sarcoid.

The patient was given x-ray therapy to the chest and femoral regions, with resultant slight reduction in the size of the lymph nodes. Six weeks after the completion of x-ray therapy the patient noticed some newly enlarged inguinal lymph nodes. At that time, however, the nodes were very painful and tender. They were fluctuant, inflamed and draining a sanguinopurulent fluid. The temperature was 102°F. There was no penile lesion. A Frei test was strongly positive. The drainage continued for 2 weeks, during which time the temperature fluctuated between 100 and 102°F. At the end of this period the lymph nodes were hard and fixed. Biopsy of one of the inguinal nodes resulted in a diagnosis of lymphopathia venereum.

Comment. This case represents one of sarcoidosis with superimposed lymphopathia venereum. The lymph nodes in sarcoidosis do not break down and the overlying skin does not shown evidence of inflammation. In lymphopathia venereum, there is also an elevation of the serum globulin, which has suggested to some observers an etiologic background similar to that of sarcoidosis. In Longcope's[20] series of cases, however, Frei tests were done in 8 cases with a positive result in only 1.

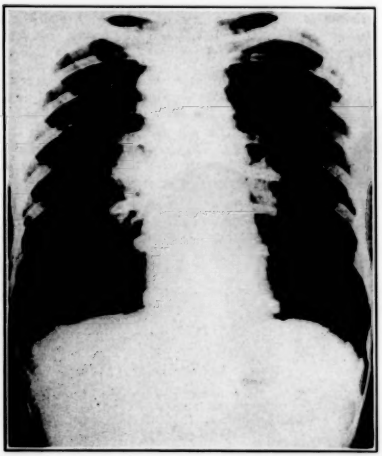

FIGURE 6. *Case 5.*
Note the bilateral enlargement of the hilar lymph nodes and mediastinal nodes.

CASE 6. An 18-year-old Negress was admitted complaining of cough and mild chest discomfort of 24 hours' duration. Her cough was productive of mucoid sputum that was occasionally blood-tinged. Slight dyspnea on exertion had been present since the onset of the present illness. Her appetite had been poor for 3 months, and during this time she had lost an unspecified amount of weight.

Physical examination revealed a well-developed and fairly well-nourished patient who was moderately dyspneic. The temperature was 99°F., the pulse 100, and the respirations 36. The blood pressure was 110/60. The scleras were icteric. Examination of the chest was negative except for slight diminution of breath sounds over the right upper lobe. The remainder of the examination was negative.

X-ray examination of the chest showed no definite evidence of infiltration of the lungs, but there was a generalized accentuation of the bronchovascular shadows. Overlying the right upper lobe there was a hazy density that was interpreted as due to a pleural reaction. X-ray films of the hands and feet were negative. A blood Kahn reaction was ++. Sputum examinations were repeatedly negative for tubercle bacilli. Intradermal tuberculin tests (P.P.D., first and second strengths) were negative. The urine showed a strong reaction for bilirubin. The red-cell count was 5,300,000, and the white-cell count 6850, with a normal differential count. The Van den Bergh reaction was direct, and there was 8.4 mg. of bilirubin per 100 cc. of blood. The icteric index was 60. The serum albumin was 2.53 gm., the serum globulin 2.26 gm., and the blood cholesterol 166 mg. per 100 cc.

The cough and chest pain subsided after 2 days. The temperature became normal on the 3rd day. At that time the patient was entirely symptom free except for slight dyspnea. Two weeks after admission an x-ray film of the chest (Fig. 7) showed diffuse irregular areas of infiltration throughout both lung fields. She felt quite well and a physical examination was negative except for slight icterus. The icteric index was 28. Subsequent x-ray examination of the chest 10 and 20 days later showed no change from the second examination.

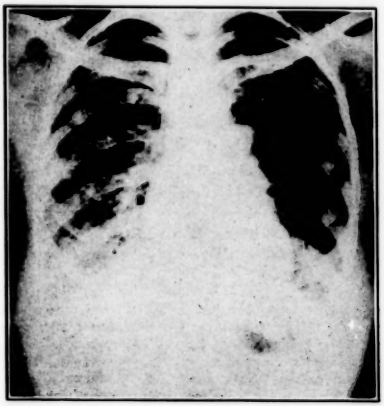

FIGURE 7. *Case 6.*
Note the diffuse irregular areas of infiltration throughout both lungs.

The patient was discharged on the 45th hospital day without any symptoms or signs, but with x-ray evidence of diffuse pulmonary infiltration. She returned at 3-week intervals for check-up examinations. After leaving the hospital she continued to feel perfectly well. X-ray examination of the chest showed no change.

Comment. In this case of sarcoidosis the pulmonary lesions developed while the patient was under observation. Although no acute symptoms are attributed to pulmonary sarcoidosis, few cases have been observed during the period of development of the lesions. The symptoms in this case may have been due to sarcoidosis or may have been manifestations of a superimposed inflammatory process.

CASE 7. A 39-year-old Negro was admitted because of cough and dyspnea. Six weeks before admission, he coughed up a small amount of blood-streaked sputum for the first time. Three weeks later, he developed a cough,

productive of mucoid sputum that was occasionally blood tinged. He continued to work for the next two weeks and then was forced to stop because of several episodes of chilliness, profuse perspiration and dyspnea.

The past history was entirely negative except for the loss of 15 pounds during the preceding year.

At physical examination the patient appeared well developed and well nourished but moderately dyspneic. The

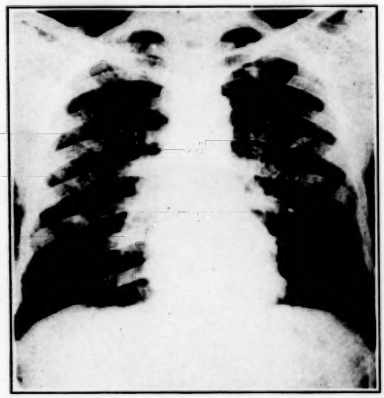

FIGURE 8. *Case 7.*

Note the small nodular areas of infiltration throughout both lungs.

temperature was 102°F., the pulse 100, and the respirations 36. There were numerous subcrepitant rales over the lower halves of both lungs. The remainder of the examination was negative.

An x-ray film of the chest (Fig. 8) showed discrete and coalescent small nodules symmetrically distributed throughout both lungs. X-ray films of the hands and feet were negative. Examinations of the sputum and gastric washings were negative for tubercle bacilli. A culture of the sputum was negative for fungi but showed sputum Types 10 and 18 pneumococci. Urinalysis was negative. The red-cell count was 4,000,000, and the white-cell count was 4200, with 61 per cent neutrophils, 36 per cent lymphocytes and 3 per cent monocytes. The serum albumin was 5.75 gm. and the serum globulin 4.11 gm. per 100 cc. An intradermal tuberculin test with P.P.D., first strength, was negative, but with second strength it was weakly positive.

The temperature remained elevated for the ensuing 2 weeks, ranging between 103 and 100°F. The cough and dyspnea improved. An x-ray film of the chest showed the same discrete nodules throughout both lungs. The coalescence previously described was no longer present. Examination of the chest at this time was negative.

During the next week the patient felt entirely well except for slight dyspnea on exertion. He remained under observation for the next 4 months, with no change in the chest x-ray or physical examination. During this period he was symptom free and gained 10 pounds. He was discharged and went back to work as a garbage collector. He has since been seen at monthly intervals. When last seen 7 months after discharge he was feeling entirely well and had gained 20 pounds. X-ray examination of the chest showed slight clearing of the discrete nodular areas of infiltration.

Comment. This is a case of pulmonary sarcoidosis with a superimposed acute inflammatory process that subsided after 2 weeks.

CASE 8. A 52-year-old Negress was admitted because of dyspnea. She had been in excellent health until 1 year before admission, when she noticed dyspnea following exertion. She consulted a physician, who attributed the dyspnea to heart failure. No benefit resulted from treatment with digitalis. The dyspnea became more severe, and she was admitted for further study.

The past history was negative except for a loss of 16 pounds during the year preceding entry.

Physical examination was completely negative.

An x-ray film of the chest (Fig. 9) showed diffuse in-

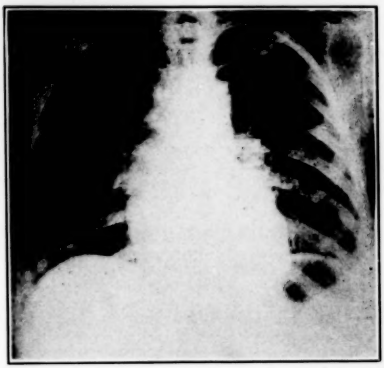

FIGURE 9. *Case 8.*

Note the diffuse mottled infiltration throughout both lungs.

filtration throughout all portions of both lungs. Films of the hands and feet were negative. Examinations of the sputum and gastric washings were repeatedly negative for tubercle bacilli. A culture of the sputum was negative for fungi. The red-cell count was 4,730,000, and the white-cell count was 4400, with 39 per cent neutrophils, 52 per cent lymphocytes, 9 per cent monocytes, 1 per cent eosinophils and 2 per cent basophils. Urinalysis was negative. The serum albumin was 2.5 gm., the serum globulin 4.3 gm., and the serum calcium 12.5 mg. per 100 cc. An intradermal tuberculin test with P.P.D., first strength, was negative, but with second strength it was weakly positive.

The patient remained symptom free except for dyspnea on exertion. X-ray films of the chest taken 2 and 4 months after admission showed no change.

CASE 9. A 27-year-old Negro had a chest x-ray film taken as a part of a routine examination. He had no

complaints and his physical condition seemed excellent. The film (Fig. 10) showed bilateral symmetrical enlargement of the hilar lymph nodes and small discrete nodules throughout both lung fields. There were also enlarged lymph nodes in the superior mediastinum on the right

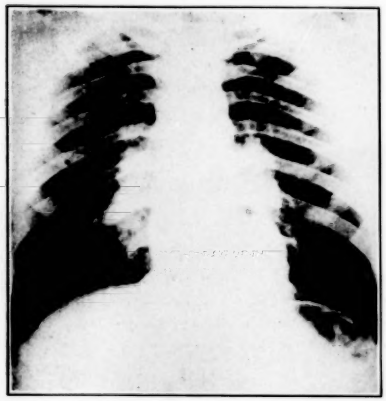

FIGURE 10. *Case 9.*
Note the bilateral symmetrical enlargement of the hilar lymph nodes and the small nodules throughout both lungs.

side. The x-ray examination was repeated 2 and 4 months later and showed no change, and the physical examination remained negative.

Examinations of the sputum and gastric contents were negative for tubercle bacilli. The red-cell count was 5,000,000, and the white-cell count 5200. The serum globulin was 2.5 gm., and the serum albumin 4.5 gm. per 100 cc. The sedimentation rate (Ernstene–Rourke method) was 1.1 mm. per minute. Intradermal tuberculin tests (P.P.D., first and second strengths) were negative.

Comment. Although in this case and in the three preceding cases the diagnosis of sarcoidosis was not proved by biopsy, the clinical course and x-ray findings in each case favored this diagnosis.

CASE 10. A 20-year-old Negress developed a nonproductive cough and dyspnea on exertion in June, 1942. She was seen by a physician, who said that she had whooping cough and prescribed various cough medicines. The cough and dyspnea continued, but were not very disturbing. In October, 1942, the patient experienced lower abdominal pain, a vaginal discharge and fever. A diagnosis of acute salpingitis was made by a physician, and one of the sulfonamide drugs was administered. Within 5 days the manifestations of acute pelvic inflammatory disease subsided. During the ensuing 4 months the cough and dyspnea became more severe. The weight in June, 1942, was 196 pounds and in February, 1943, it was 141 pounds. Because of this weight loss, cough and dyspnea, the patient was referred by her physician to a hospital. Following x-ray examination of the chest she was transferred to the Gallinger Municipal Hospital with a diagnosis of miliary tuberculosis.

The past history revealed "rheumatism" at the ages of 13 and 15. Since the age of 17 the patient had had episodes of polyarthritis lasting several days. An appendectomy had been performed at 13 years of age, and a tonsillectomy at 14. She had had a 6-month spontaneous abortion at the age of 16.

At physical examination the patient was well nourished and well developed and did not appear to be ill. She was slightly dyspneic and coughed every few minutes. The temperature was 98.6°F., the pulse 100, and the respirations 35. The only positive findings were occasional subcrepitant rales over the lower halves of both lungs and bilaterally palpable epitrochlear and axillary lymph nodes 1 cm. in diameter.

An x-ray film of the chest (Fig. 11) showed diffuse, discrete and coalescent miliary nodules throughout both

FIGURE 11. *Case 10.*
Note the miliary nodules throughout both lungs.

lungs. In the right superior mediastinum there was a large lymph node and in both hilar areas the infiltration was more homogeneous. X-ray films of the hands and feet were negative. The red-cell count was 4,980,000 and the white-cell count 6100, with 51 per cent neutrophils, 31 per cent lymphocytes, 5 per cent eosinophils and 1 per cent basophils. Examinations of five sputums and one gastric washing were negative for tubercle bacilli. Culture of the sputum was negative for fungi. Intradermal tuberculin tests (P.P.D., first and second strengths) were negative. The serum calcium was 11.2 mg., the serum albumin 4.77 gm. and the serum globulin 3.72 gm. per 100 cc. Urinalysis was negative. The sedimentation rate (Ernstene–Rourke method) was 0.6 mm. per minute. A blood Kahn reaction was negative. A biopsy of the right epitrochlear lymph node showed the typical findings of sarcoid.

The patient remained in the hospital for 7 weeks. During that time she gained 10 pounds and felt well except for exertional dyspnea and cough. The temperature was normal throughout her stay. One week after discharge she returned to the hospital complaining of severe malaise,

fever, sore throat and headache of 24 hours' duration. On the evening before admission she had had a shaking chill.

At physical examination the patient was seen to be acutely ill. The temperature was 104°F., the pulse 160, and the respirations 70. Subcrepitant rales were heard throughout both lung fields. A culture of the sputum showed Type 7 pneumococcus, and a blood culture was negative. The remaining laboratory studies showed no significant change from the previous admission. X-ray examination of the chest showed no appreciable change from the previous examination with the exception of a slightly greater degree of coalescence of the nodules.

The patient was given sulfadiazine, and within 48 hours the temperature was normal, the pulse 100 and the respirations 34. She has remained afebrile and asymptomatic with the exception of slight cough and exertional dyspnea.

Comment. This case shows the ease with which sarcoidosis may be mistaken for miliary tuberculosis from the roentgenologic point of view. On the other hand, the absence of severe constitutional manifestations in the presence of diffuse pulmonary disease should lead one to the correct diagnosis. The superimposed bronchopneumonia is not an uncommon finding in sarcoidosis. The polyarthritis may also have been due to sarcoidosis.

Summary

The concept of sarcoidosis as a generalized systemic disease is traced in the literature, and its cause and manifestations are discussed.

Arguments for and against a tuberculous origin of the disease are presented. The syndrome is also found in leprosy.

The fact that neutropenia and leukopenia may occur suggests that a virus is the etiologic agent, but the etiology remains obscure.

Clinically, sarcoidosis is characterized by widespread involvement of organs, with few constitutional manifestations. The commonest initial finding is enlargement of lymph nodes. Pulmonary and bone lesions are common. There is wide variation of syndromes.

The laboratory findings, course, diagnosis and treatment are discussed.

Ten typical cases are briefly reported.

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CLINICAL NOTES

THE USE OF DALIBOUR'S WATER IN THE TREATMENT OF SKIN DISEASES

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DALIBOUR'S water has been used by French dermatologists in the treatment of traumatic wounds and pyogenic infections of the skin for almost two hundred and fifty years. A weak solution of copper sulfate and zinc sulfate, it is an excellent astringent, bacteriostatic and deodorant. It deserves more widespread use in this country than it is receiving, both because of its obvious intrinsic worth and because in dermatological therapy it can be substituted with advantage for many of the other heavy metals — aluminum, silver and so forth — that are needed in the war effort.

The name has been spelled many different ways, including "Auillebourst,"[1] "D'alibourst" and "D'alibourt." In all official papers, however, the spelling has been "Dalibour," and the latest edition of the French pharmacopoeia has reaffirmed this form.

The water or solution was first described by Jacques Dalibour in 1700.[2] The formula of the *"l'eau de merveille"* was kept a family secret until 1812, when its composition was revealed in the *Formulaire Magistrale*. It is as follows:

℞	Copper sulfate	0.1 gm.
	Zinc sulfate	0.4 gm.
	Safranine	0.1 gm.
	Camphor water	1.0 cc.
	Water *q. s. ad*	100.0 cc.

Sig. Dilute with three or four parts of water and apply as a wet dressing or compress.

When large quantities are to be used, a ten-times concentrated solution is more convenient and economical. This should be diluted before use with twenty to forty parts of water.

The solution is clear, odorless and pink, is astringent, and has a mild metallic taste. The pH varies from 5.3 to 6.3.

Combes[3] has said:

> The logic of Dalibour's reasoning in compounding this solution is simple and clear. The local therapeutic value of copper sulfate and zinc sulfate was recognized by physicians many centuries before boric acid and aluminum acetate were known. Blue or Roman vitriol water in the fourteenth and fifteenth centuries was extolled as a local wet dressing in cutaneous inflammations and impetigo. The same may be said of white vitriol, which found its broadest use as a collyrium in inflammations of the conjunctiva. Copper sulfate, in addition to possessing local stimulating and astringent properties, even in high dilutions is bacteriostatic and fungicidal.
>
> Camphor is highly prized in the household as a local sedative. Aqua sedativa is an old item in the *National Formulary*, its antipruritic and sedative properties being dependent upon its camphor content. . . .
>
> The simultaneous application of copper and zinc sulfates and camphor by means of Dalibour water affords us an effective bacteriostatic, astringent and sedative solution for use as a wet compress.

Many modifications of the original formula are possible. The addition of 1 per cent gentian violet or 1 per cent brilliant green increases the bacteriostatic properties. Omission of the safranine permits the dispensing of a light blue solution. From 0.5 to 1.0 per cent of formalin may be included to enhance the astringent effect, or alcohol may be substituted for part of the water to further the solution's drying and astringent characteristics. Many similar alterations can be made and will readily come to mind.

When employed in the form of a wet dressing or wet compress, Dalibour's water is an effective remedy for superficial pustular infections of the skin. It is especially useful in the therapy of secondarily infected epidermophytosis, scabies or pediculosis corporis. It is equally valuable in the treatment of impetigo contagiosa, nummular eczema, superficial erosions and varicose ulcerations. Such use effects prompt control of the infectious process, thus permitting early definitive therapy for the underlying condition — scabies, epidermophytosis and so forth.

The water can be incorporated readily in such widely used preparations as lanolin, zinc oxide paste *N. F.* and bentonite paste, or in one of the newer oxycholesterin or glyceryl monostearate creams. The following formulas are suggested:

℞	Copper sulfate	0.04 gm.
	Zinc sulfate	0.15 gm.
	Water	3.00 cc.
	Lanolin	10.00 gm.
	Zinc oxide paste *N. F.* *q. s. ad*	30.00 gm.

Sig. Apply to oozing parts.

℞	Copper sulfate	0.3 gm.
	Zinc sulfate	0.9 gm.
	Urea	12.0 gm.
	Aerosol OT (25 per cent)	0.2 gm.
	Bentonite	20.0 gm.
	Water *q. s. ad*	120.0 cc.

Sig. Apply to ulcers.

As a deodorant it is unsurpassed for the therapy of severe odorous cancerous lesions, condyloma acuminatum or epidermophytosis. In weak dilutions, either as a compress, in a vanishing cream or applied by atomizer to the axillas before bed-

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time two or three times a week, it is effective in the relief of hyperidrosis and bromidrosis.

A mixture of copper sulfate and zinc sulfate may be prescribed in powder form for the bath. Thirty parts of copper sulfate and 90 parts of zinc sulfate are mixed and pulverized, and from a teaspoonful to a tablespoonful of the powder is dissolved in water and added to the bath. Such baths are astringent and bacteriostatic and efficiently remove odor from patients suffering with pemphigus vulgaris, ulcerating cancer or other malodorous conditions. The patient is allowed to remain in the tub from ten to thirty minutes. Since elderly patients may develop cerebral anemia and may faint in prolonged warm baths, they should be watched constantly. Unlike potassium permanganate, Dalibour's powder does not permanently stain the tub or skin. Patients who have taken both permanganate and Dalibour baths strongly prefer the latter.

It must not be thought that Dalibour's solution is a panacea for skin diseases. It has proved of no value in deep-seated pustular follicular diseases, such as acne vulgaris, sycosis vulgaris and furunculosis. Solutions of aluminum acetate and silver nitrate have proved better therapeutic agents where astringency is primarily desired, as in non-infected dermatitis venenata, eczema and so forth. Despite these shortcomings, however, Dalibour's water and its many possible modifications are valuable therapeutic agents and deserve more widespread use.

520 Commonwealth Avenue

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"DRY ICE" BURN OF THE HYPOPHARYNX

Report of a Case

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THE following case of a burn of the hypopharynx is reported because of its unusual etiology. "Dry ice" (solid carbon dioxide) is a caustic agent, to be classed with lye, in that it may be as dangerous as the latter when it attacks the mucous membranes, particularly in the airway and esophagus. Two similar cases were found in the literature.[1,2] In the first one, tracheotomy was performed, whereas in the second one, as in the case reported below, the patient recovered without serious complications.

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Case Report

W. H., an 11-year-old boy, was admitted to the Faulkner Hospital on May 31, 1942, within 30 minutes after swallowing a teaspoonful of "dry ice" in an effort to imitate his elders smoking. Marked vomiting and expulsion of most of the "dry ice" followed promptly, but considerable difficulty in swallowing and some labored respiration persisted.

Examination of the mouth was negative. There was marked edema of the base of the tongue, hypopharynx and arytenoid cartilages. The vocal cords were normal, and respiration was adequate.

Treatment consisted of absolute bed rest. One teaspoonful of albolene was given by mouth every 4 hours. The taking of food and water by mouth was stopped. Frequent mouth washes with dilute Dobell's solution were given. The patient was closely watched, and a tracheotomy set was kept at hand in case of continued edema of the larynx.

Subsequent progress was satisfactory and the edema subsided within 4 days. Since there was considerable secondary infection, a culture showing hemolytic streptococci, with some elevation of temperature, 1 gm. of sulfadiazine was given every 4 hours, beginning on the 3rd day. After a blood level of 4.0 mg. per 100 cc. had been obtained, the dose was reduced to 0.5 gm. three times a day for 2 days, and then stopped. The patient was discharged June 7 with the temperature normal; he was able to swallow small amounts of fluids with comfort.

Two weeks after the onset, x-ray and fluoroscopic examination of the esophagus showed only a possible delay in swallowing. Since the patient was eating strained vegetables and soft solids with no discomfort, no further examination of the esophagus was made. Indirect laryngeal examination 3 weeks after the onset was negative. The patient felt well, had returned to school, and was eating as usual. Fluoroscopic and film x-ray examinations 3 months after the accident showed no deviation from normal.

270 Commonwealth Avenue

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MEDICAL PROGRESS

CHEMICAL FACTORS IN INFLAMMATION AND CELLULAR INJURY*

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OWING to limitations of time, the following discussion will be confined to certain aspects of recent studies on inflammation in this laboratory. The subjects to be dealt with are the concept of increased capillary permeability and the mechanism involved, which has led to the identification of leukotaxine in inflammatory exudates; the studies on the isolation of the leukocytosis-promoting factor; some chemical factors that condition the cellular picture in inflammation; and a brief review of the latest studies on the factor concerned in explaining the basic pattern of cellular injury in inflammation, which has led to the view that the stereopattern reaction of injury in inflammation is referable to the liberation of necrosin.

Inflammation is a manifestation of severe cellular injury, and as such represents the basis of all infectious processes. It can be readily defined as the complex vascular, lymphatic and tissue response on the part of vertebrate tissue to the presence of an irritant.[1‡] An irritant may be considered to be any agent that interrupts normal cellular metabolism. It may be physical in nature, chemical or viable, as in the case of micro-organisms.[2]

Inflammation consists of a number of interdependent sequences that lead to the localization and ultimate disposal of the irritant. These phases are often grouped under the somewhat loose term "inflammatory reaction." Initially, there is a disturbance in fluid exchange, manifested by an alteration in the normal equilibrium of capillary filtration. There is at first, as shown by Landis,[3] a transitory increase in capillary pressure, and this is followed by more permanent changes in the structure of the endothelial wall structure — namely, augmentation in its permeability.[4] The enhancement in permeability can be readily demonstrated by introducing trypan blue into the circulating blood of a rabbit. The area of injury is rapidly stained blue owing to the outward passage of the dye.[2] The magnitude of increase in permeability is such as to allow particulated material to pass into the extra-capillary spaces.[5] The extent of increased capillary permeability is subject to measurement. A number of years ago it was shown that, on introducing a dye into the ventricle of a pithed frog with its mesenteric capillaries exposed on the stage of a microscope, — one could evaluate with an appropriate scale the rate of change of concentration of the dye as it passes out into the extra-capillary spaces.[6] It was found that with inflammation caused by certain irritants the permeability of capillaries is enhanced about twofold.

LEUKOTAXINE AND THE MECHANISM OF INCREASED CAPILLARY PERMEABILITY

The mechanism of increased capillary permeability in inflammation is an important factor, for it is the pivotal reaction on which all subsequent sequences depend. Lewis[7] about twenty years ago, stimulated by the work of Ebbecke, postulated that the phenomenon is referable to the liberation of histamine or at least to a substance so closely allied to it that he termed it the "H-substance."[7] The argument utilized by Lewis is fraught with difficulty, for it is largely one of analogy. For this reason the whole problem was reinvestigated several years ago in this laboratory. It was readily shown that the exudative fluid recovered from the site of inflammation contains a factor in turn capable of eliciting an increase in capillary permeability.[8] This could be readily demonstrated by the seepage of a dye from the circulation into an area of skin previously inoculated with a sample of exudative material. Subsequently, chemical extraction was undertaken by first eliminating the protein fraction of exudates by treatment with pyridine and acetone. The acetone supernatant phase after desiccation is treated with butyl alcohol. The active material when kept at a low temperature comes down in the butyl alcohol phase after concentrating the latter. The material usually appears in the form of doubly refractive aggregates that at times and with proper desiccation from an aqueous medium appear in the form of needle crystals.[9] This powerful substance, capable

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‡The references cited herein pertain primarily to the various studies of the writer. A more complete bibliography appears elsewhere.[2]

of inducing an increase in capillary permeability in a dilution of 1:100,000, or even in greater dilution, has been termed "leukotaxine." It is evidently not a protein. It has an α-amino group and an indole nucleus. There is evidence that it is a polypeptide to which a prosthetic group may be attached.

Leukotaxine readily diffuses out of a cellophane tube. It has none of the properties of histamine, thereby throwing considerable doubt on the view of Lewis that H-substance is primarily concerned in the mechanism of increased capillary permeability in inflammation. The whole exudate elicits the capillary reaction. Laborious extraction yields a crystalline-like substance that reproduces exactly a pattern similar to that caused by the untreated exudate. Yet the substance has none of the properties of histamine. This to a large extent invalidates the Lewis hypothesis. Leukotaxine, in contrast to histamine, fails to contract the isolated segment of guinea-pig intestine.[9] Extracting leukotaxine for the possible presence of histamine by the method of Barsoum and Gaddum[10] fails to yield any evidence that the latter is present.[11] Leukotaxine fails to depress the blood pressure in a cat, in contrast to the marked depressant effect of histamine.[12] It is evidently not histamine, or acetylcholine, since it fails to lower blood pressure. The following test indicates that it is probably not an adenylic compound. Parnas and Ostern[13] have reported that adenosine induces heart block in the frog. Leukotaxine completely fails to induce any such arrhythmia.[12] Leukotaxine can evidently induce an increase in the permeability of cells in general, even among lower invertebrates. This is of significance, for it indicates the wide biologic value of this substance. For instance, it increases by about 50 per cent the permeability of the ova of the sea urchin (*Arbacia punctulata*) to sea water. This superficial effect doubtless induces a minor degree of cellular injury, for the fertilization of such eggs is followed by a retardation in cleavage development, together with atypical cleavage.[14] In such ova the fertilization membrane is closely adherent to the cell, and numerous sperms are firmly attached to the membrane.

The increase in capillary permeability induced by leukotaxine has been found to be counteracted by only one substance — namely, the extract of the adrenal cortex — and to a certain extent by some of the steroid compounds derived from the adrenal cortex.[15–17]

Leukotaxine is concerned with another fundamental manifestation in inflammation — the migration of polymorphonuclear leukocytes to the site of injury.[18] This is often referred to as chemotaxis. The ideas of Abramson[19] on the subject, although perhaps attractive as such, have unfortunately received little experimental support, either in his hands or in those of other investigators. The conclusions are primarily unsupported assumptions. The views of this worker consist in assuming that negatively charged leukocytes in an electronegative blood stream readily migrate, as in a cataphoretic chamber, into a positively charged area of connective tissue that has previously been injured. Leukotaxine does not as yet explain the exact intrinsic cellular mechanism concerned in the motion of leukocytes, but it at least stands out as a concrete substance, liberated in exudates, that is definitely chemotactic. This fact in itself offers the distinct possibility of attacking the problem further in an endeavor to determine how leukotaxine specifically affects the mobility of white cells so as to induce their migration to the site of inflammation. Whether electric charges have anything to do with the phenomenon remains to be proved. The end product of blood serum extracted for leukotaxine yields no activity so far as cell migration is concerned. On the other hand, leukotaxine derived from exudates is definitely chemotactic, for its injection into tissues induces not only a marked increase in capillary permeability but also a distinct migration of polymorphonuclear cells outward into the area of injury. The chemotactic property of leukotaxine can be easily demonstrated by in vitro observations.[2] The placing of leukotaxine crystals on a slide containing a drop of exudate is soon followed by migration and clustering of cells at the periphery of particles of leukotaxine. No such effect is observed with either carbon particles or reduced iron powder.

In conclusion, leukotaxine extracted from inflammatory exudates offers a reasonable explanation for two of the basic sequences in inflammation — namely, the mechanism of increased capillary permeability and the local migration of polymorphonuclear leukocytes. Besides these two functions, leukotaxine appears to be relatively innocuous so far as the induction of any appreciable tissue injury is concerned.

The Mechanism of Leukocytosis with Inflammation

The leukocytosis-promoting factor is another potent biologic substance recently isolated from the site of inflammation. Leukotaxine introduced into the circulating blood fails to alter the number of white cells.[20] Yet it is well known that in numerous inflammatory processes the level of circulating leukocytes is considerably elevated. The leukocytosis has been shown to be referable to a chemical unit.[20] The injection of whole exudative material into the blood stream of a dog induces a prompt leukocytic response. Neither leukotaxine nor blood

serum is capable of eliciting such a reaction. The evidence indicates that there is a leukocytosis-promoting factor present in inflammatory exudates. This factor in contrast to leukotaxine is nondiffusible, and it is thermolabile.[20] Its injection is accompanied by a discharge of immature leukocytes into the circulation. Chemical extraction of exudates

FIGURE 1.

This drawing of a section through the femoral bone marrow of a dog that had received several days previously an injection of the pseudoglobulin fraction derived from normal blood serum shows that the marrow is essentially normal.

yields activity in the pseudoglobulin fraction.[21] Other protein fractions such as albumin and euglobulin are ineffective in inducing a state of leukocytosis. The material is absent in normal blood serum, but can be recovered from the serum of an animal with a concomitant inflammation.[22] This fact suggests that it reaches the bone marrow by way of the blood stream. The material can be obtained from the exudates of dogs and rabbits[2, 23] and of human beings.[24]

The most recent finding in connection with the leukocytosis-promoting factor is its capacity not only to discharge immature granulocytes into the circulation but also to induce a marked and specific growth effect in the bone marrow.[25, 26] The result is a conspicuous hyperplasia of some of the hematopoietic elements, notably the granulocytes and the megakaryocytes (Figs. 1 and 2).

In brief, the leukocytosis-promoting factor of exudates offers a reasonable explanation for the mechanism of leukocytosis accompanying numerous inflammatory processes. Its marked growth effect on some of the elements of the bone marrow obviously may prove to have clinical implications. These require no further comment.

Cytologic Sequence in Inflammation

Another fundamental sequence in the development of the inflammatory reaction is the initial infiltration of polymorphonuclear leukocytes, which are subsequently replaced by macrophages. This is an almost invariable cytologic sequence.[27-29] With some irritants the polymorphonuclear phase may be lengthened and the macrophage one correspondingly shortened — for example, staphylococcal abscess — or vice versa — for example, the tubercle. Nevertheless, the same basic principle is maintained. Several years ago it was observed

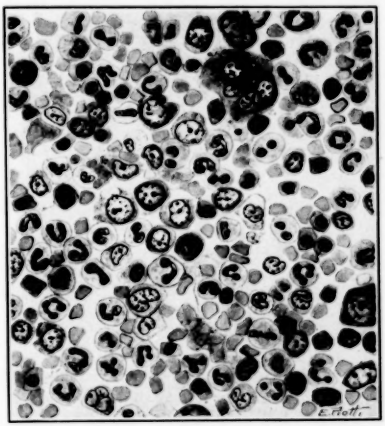

FIGURE 2.

This drawing of a section through the femoral bone marrow of a dog that had received several days previously an injection of 87 mg. of leukocytosis-promoting factor derived from exudative material shows an extensive hyperplastic response replacing the usual areas of adiposity. A mitotic figure is in evidence. The factor seems to stimulate primarily the growth of granulocytic elements and of megakaryocytes.

that this phenomenon is referable to a developing local acidosis at the site of an acute inflammation.[30] In earlier studies it was demonstrated that the local circulation in an inflamed area is markedly impaired.[31] The lymphatic outlets become occluded, and in time thrombi are also found in

the smaller vascular channels. Thus, the area of inflammation becomes, so to speak, shunted from the rest of the organism. It develops its own hydrogen-ion concentration, its own circulation and its own metabolism. The polymorphonuclear leukocytes brought to the site of injury through the action of leukotaxine, as described above, are unable to survive below pH 7.0, whereas the mononuclear phagocytes appear fairly normal at pH 6.9 to 6.8. At a somewhat lower pH all types of leukocytes tend to be injured. The result is a state of suppuration. Pus is virtually a function of the hydrogen-ion concentration. For instance, a twenty-four-hour exudate from the pleural cavity of a dog previously injected with turpentine is primarily composed of polymorphonuclear leukocytes, whereas an exudate of several days' duration at pH 6.5 reveals an absence of normal polymorphonuclear cells. The rise in hydrogen-ion concentration tends to precede the change in the differential leukocyte picture. On the other hand, if the reaction remains alkaline during the development of the inflammatory reaction, the cellular picture is characterized throughout by a predominance of polymorphonuclear leukocytes. That the general effect is an inability on the part of polymorphonuclear leukocytes to survive at an acid reaction has been demonstrated by subjecting leukocytes in vitro to buffers at various hydrogen-ion concentrations.[32] In this way it is readily shown that these cells tend to cluster and become swollen with coarse granulation at about pH 6.5. When supravitally stained, the nuclei take up the dye, indicating severe injury. These changes are absent in cells exposed to pH 7.4.

It is of importance to determine the mechanism of local acidosis with inflammation if one is to comprehend the forces at work in conditioning the cytologic picture at the site of an acute inflammation. The alkali reserve of the exudate tends to decrease with the developing local acidosis.[33] This in itself might be expected to occur, for it is another means of expressing the rise in hydrogen-ion concentration. Incidentally, it is well to emphasize again that all the biochemical changes are local; the reaction of the blood remains essentially unaltered.

The local acidosis seems to be primarily referable to a glycolytic process.[33] The result is a true lactic acid acidosis. Several chemical variables have been studied in the exudate during the progress of the inflammatory reaction. These include the concentration of sugar and of lactic acid and the measurement of the pH, correlated in turn with the cellular picture. The conversion of glucose to lactic acid induces a local acidosis, with the resulting effect on the leukocytes described above.

In conclusion, the cellular picture in inflammation is primarily conditioned by the hydrogen-ion concentration, which in turn seems to be referable to a disturbance in the intermediary carbohydrate metabolism. The lymphocytes appear to be unaffected — at least directly — by the changes in hydrogen-ion concentration. The function of the latter cells is still somewhat obscure. The studies of McMaster and Hudack[34] and the more recent work of Ehrich and Harris[35] suggest their possible role in the formation of antibodies.

Diabetes and Inflammation

The biochemical studies on the relation of hydrogen-ion concentration to the cellular picture at the site of an acute inflammation have led to further extensive investigation in an attempt to unravel the mechanism concerned in the intensifying of the diabetic state when there is a superimposed inflammation in depancreatized dogs.[36] Time forbids discussion of the details of this work. Suffice it to say that an inflamed area is a focus of proteolysis. At the site of inflammation in a diabetic animal the breakdown of proteins is considerably exaggerated. Local gluconeogenesis from the deaminated part of the protein molecule readily explains the heightening in blood sugar following the diffusion of glucose previously formed at the site of injury. Close analysis indicates that in general, even in nondiabetic animals, glucose is capable of being formed by injured cells.[37] Such cells are therefore potentially foci of gluconeogenesis. The process is merely exaggerated in the diabetic animal. There is also some additional evidence that urea, besides originating in the liver, is likewise formed at the site of an acute inflammation.[37]

The Chemical Basis of Injury in Inflammation

The last phase of the most recent studies to be considered here is the presence of a fundamentally stereopattern of injury in the development of the inflammatory reaction, irrespective of the irritant. The latter and the anatomic location of the lesion may modify its ultimate appearance. Nevertheless, close scrutiny reveals a basic pattern of injury. For instance, damaged cells may show granular elements strewn through their cytoplasm; the cells may be vacuolated; the collagenous bundles may appear swollen; and the nuclei may reveal various degrees of pyknosis. Another evidence of tissue injury found in a variety of acute inflammatory lesions is displayed by the fibrinous occlusion of lym-

phatics and also by the presence of small thrombi in the blood vessels of an inflamed area.[1]

It may be asked whether the mechanism that accounts for the basic pattern of injury in inflammation is referable to a chemical unit. Leukotaxine scarcely induces any degree of injury to cells except for an augmentation of cellular permeability. The leukocytosis-promoting factor elicits essentially no injury to tissues. Recent studies, however, have indicated that the euglobulin fraction of exudates is highly injurious to the cutaneous structures of the rabbit and to some extent to those of the dog.[38] There is thus an accumulated body of evidence that either in the euglobulin fraction of exudates or else associated with it there is present an injury factor capable per se of reproducing the nocuous effects seen in inflammation. This substance or factor has for the sake of convenience been termed "necrosin."[38] Its injection into the skin of rabbits is accompanied by intense redness, edema and usually a central area of necrosis. No other fractions of exudate appear to be capable of inducing any such effect. Furthermore, the euglobulin fraction of normal blood serum elicits absolutely no appreciable lesion in the skin of rabbits. On the other hand, the same fraction from the serum of a dog with a concomitant acute pleural inflammation frequently induces a severe inflammation. This observation suggests that the toxic substance is absorbed from the site of inflammation into the circulation, whence it can be recovered. This fact is perhaps of significance in re-evaluating the concept of a focus of infection and its far-reaching repercussions to other organs.

Necrosin induces an acute inflammation with blockade of the lymphatics. A section through such an area reveals zones of dense leukocytic infiltration in which the lymphatic channels may be occluded by thrombi.[39] Small vascular channels may also show evidence of thrombosis. On the other hand, the euglobulin fraction of normal serum leaves the lymphatic channels essentially patent. About ten minutes after the injection of necrosin into the skin of rabbits the collagen bundles often appear to be swollen, with a tendency to fuse together. The latter seems to be one of the first morphologic evidences of the injurious effect of necrosin on supporting structures.

As stated previously, necrosin can be recovered from the blood serum of an animal with an acute inflammation. This interesting observation, which may reasonably explain the toxic effect of a lesion on organs at a distance, has suggested the necessity of examining the generalized effect on organs of an intravenous injection of necrosin.[39] Although several organs, such as the gastrointestinal tract, may show evidence of injury, or various lymphoid structure may reveal signs of enlargement and congestion, it is nevertheless only the liver and to some extent the kidneys that seem most frequently to exemplify signs of damage. Many of the parenchymatous cells of the liver appear swollen and contain many fat vacuoles. There are interspersed foci of leukocytic infiltration, reminiscent of hepatic focal necrosis. The liver on gross examination is streaked with what seems to be yellowish or whitish foci. In some cases the cell outlines have disappeared and the liver cords are stippled with coarse, black-stained granules that do not take the iron stain. The epithelial lining of the kidney tubules may show irregularities and vacuolation, and foci of leukocytic infiltration separating some of the tubular structures may also be present.

Various investigators[40, 41] who have studied the problem of traumatic or surgical shock have arrived at the conclusion that one or several toxic substances are absorbed into the circulation from the site of acute injury. It is indeed quite conceivable that in the syndrome of shock there are several such substances, and furthermore that the clinical picture of shock is to a large extent due to some of these substances in addition to superimposed systemic neurologic factors and to an alteration in the blood volume. At any rate, necrosin per se fails to depress the blood pressure in a cat, in contrast to the action of histamine.[39] It is quite conceivable that in shock the fall in vascular tension is referable to histamine, whereas the other noxious effects are due in part to the liberation of necrosin at the site of injury.

There are two additional properties of necrosin that indicate its significance to the student of pathology. Its intravenous injection into a dog is accompanied by severe toxic manifestations, including vomiting and diarrhea. For a while the animal lies on its side and appears somewhat prostrated. Of greater significance is the abrupt fall in the number of circulating leukocytes, which is usually extremely marked. The white-cell count may fall in an hour or two from about 10,000 to 1000 or 2000. After several hours the dog appears to be clinically improved and the white-cell count rises. Subsequently or on the following day a leukocytosis may ensue. It is conceivable that the latter is a secondary effect caused by the initial injury of various organs by necrosin, which thus allows the release of the leukocytosis-promoting factor. The inability of other fractions of exudate to induce leukopenia suggests that the liberation of necrosin at the site of injury and its absorption into the blood stream are actively concerned in the mechanism of the developing leukopenia accompanying certain infectious processes.

Of perhaps even greater interest is the fact that the intravenous injection of necrosin in dogs is accompanied by a marked rise in temperature simul-

taneous with the developing leukopenia, possibly of 3 to 5°F. The early studies of Grafe[42] suggested that in infectious processes the fever is referable to the absorption of products of cellular disintegration. Other protein fractions of exudate — for example, the leukocytosis-promoting factor or the euglobulin fraction of normal serum or of ascitic fluid — are all incapable of inducing any fever when injected into the circulating blood of a dog. The fact that necrosin seems to be the only fraction to have this capacity suggests strongly its possible role in the production of fever with inflammation.[39]

Summary and Conclusions

The presence of leukotaxine, the leukocytosis-promoting factor and necrosin in inflammatory exudates offers a reasonable explanation for the development of a fundamental pattern in inflammation. Observations suggest that an irritant irrespective of its nature severely injures cells, which in turn, as a result of their deranged metabolism, liberate various common denominators — for example, leukotaxine, the leukocytosis-promoting factor and necrosin. These substances, which are to be regarded as constant products of marked cellular injury, are responsible for the recognized pattern of the inflammatory reaction.

The salient sequences in inflammation besides the basic injury caused by the presence of necrosin may be recapitulated as follows[2]:

(1) *Disturbance in local fluid exchange.*

(*a*) Increase in capillary permeability, which is primarily referable to liberation of leukotaxine.

(*b*) Initial increase in lymph flow.

(2) *Localization of the irritant (fixation).*

Time has prevented any discussion of this earlier work, which has led to the view that inflammation is the regulator of bacterial invasiveness through its ability to induce blockade[1] of the lymphatics. Thus, the dissemination of a micro-organism bears in large part an inverse function to the induced degree of local injury and a direct function to time.

(3) *Migration of leukocytes.*

(*a*) The diapedesis of polymorphonuclear leukocytes is referable to the liberation of leukotaxine.

(*b*) The cytologic sequence at the site of an acute inflammation is conditioned by the local hydrogen-ion concentration.

(*c*) The leukocytosis in the circulating blood stream is referable to the liberation at the site of inflammation of a pseudoglobulin, the leukocytosis-promoting factor.

The interplay of the foregoing sequences favors the localization and the ultimate disposal of the irritant. This leads to the final reparative phase of the injured area. There are suggestive observations that repair may also be due to the liberation of growth-promoting factors by mildly injured cells.[43] Necrosin seems to be released by the cell that is severely injured by an irritant, and thus the appearance of necrosin initiates the inflammatory process. Its chemical separation from the rest of the exudative fluid becomes a necessity in any endeavor to determine whether proliferative or reparative factors derived from probably less severely injured cells are likewise present in exudates. Such studies are now under way.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

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CASE 29381

PRESENTATION OF CASE

A fifty-one-year-old man, a factory worker, entered the hospital because of acute abdominal pain.

One week prior to admission the patient developed upper abdominal "distress," the nature of which he was not able to describe well. It was apparently not related to food. There was no associated back or shoulder pain, nausea or vomiting, but he was forced to stop working. His bowel movements had been fairly normal with a laxative prescribed by his physician. At the onset of his present illness he contracted a "cold" after removing storm windows. There were no chills, fever, urinary disturbances or chest pain. He had remained in bed more or less constantly. On the night before admission the pain in the abdomen became worse and he developed chilly sensations. He was given a hypodermic by his doctor and sent into the hospital. There was no vomiting. His last bowel movement had been two days before admission, at which time he had two loose stools. He had not passed gas by rectum since then.

Physical examination disclosed a moderately obese man with questionable cyanosis of the lips and fingernails. The skin was moist. The heart was not enlarged. A short systolic murmur was heard in the aortic region, which was not transmitted. The aortic second sound was greater than the pulmonic. The heart rate was regular and of good quality. The lungs were clear. The abdomen was flat. No peristalsis could be detected anywhere. There was voluntary spasm all over, but when the muscles were relaxed by flexion of the legs, there was variable response to palpation — once it was "sore," then "no pain," then "a little tender" and so on. No definite masses were felt. There was no costovertebral tenderness. Rectal examination showed no tenderness or masses. The prostate was slightly enlarged. There was no edema or ascites.

*On leave of absence.

The blood pressure was 158 systolic, 80 diastolic. The temperature, pulse and respirations were not recorded.

Urine examination was negative. Examination of the blood showed a white-cell count of 16,200, with 84 per cent neutrophils. Three hours later the white-cell count was 11,300. A blood Hinton test was negative. An electrocardiogram was interpreted as showing normal rhythm, at a rate of 80, with low T_2 and total inversion of Lead 3; Lead 4 was normal.

A roentgenogram of the abdomen showed considerable gas and fecal material in the proximal colon. The colon distal to the splenic flexure was collapsed. A film taken on the following day in the prone and upright positions showed several dilated loops of small bowel on both sides of the midabdomen as well as a large, single loop of bowel that appeared to be small intestine. There was also a small amount of gas in the colon in the region of the splenic flexure. An upright film showed fluid levels within several of the loops on the right side of the abdomen. There was no air beneath the diaphragm. A barium enema on the second hospital day revealed the passage of barium to the cecum and the terminal ileum without delay. There was a moderate amount of fecal material within the colon that somewhat hindered the examination. No gross evidence of obstruction or definite evidence of ulceration or of a filling defect could be seen. There were two loops of slightly dilated air-filled small bowel in the left midabdomen. Barium passed through the ileum to the air-filled loops of bowel, and one loop gave the appearance of partially encircling a mass over the left side of the lumbosacral junction; the loop in question was somewhat narrowed and irregular in outline.

An electrocardiogram on the third hospital day was normal.

On the third hospital day the patient had a spontaneous bowel movement. Peristalsis was audible, and the abdomen flat. On further questioning it was brought out that the patient had had two former episodes of substernal pressure with radiation down the left arm, lasting three to five minutes and coming on while he was working on a chair. These attacks had been diagnosed as angina pectoris and the patient was advised to live a moderately restricted life. Since then the patient had had no similar episodes.

A gastrointestinal series on the fifth hospital day showed that the passage of barium through the pylorus was very slow. A large residue of barium was seen in the colon, especially in the region of the cecum, which was dilated. There was considerable gas in the hepatic and splenic flexures. Hourly films showed slow passage of

barium to the small bowel, and for a period of three hours no progression was seen. The stomach was almost completely empty at three hours, and all the barium was found to be in a few loops of small intestine on the left side of the abdomen in the region where the air-filled loops were visible on the previous examination. At four hours, however, barium had passed through the narrowed loops previously described. Spot films taken over this region showed no definite evidence of ulceration. The narrowing was believed to have been due to extrinsic pressure. At four hours the head of the barium meal was in the region of the ileocecal valve, but had not entered the cecum. No mass could be definitely visualized.

Following the gastrointestinal series the patient was given an enema, with good results. He was seen twice that evening and appeared well. At about 4:00 the following morning he began to complain of gas pains, and another enema was given. Soon after that the patient was found to be sweating profusely. The blood pressure could not be obtained. The abdomen was slightly distended. The pulse was about 120. Examination of the blood revealed a white-cell count of 29,800, with 87 per cent neutrophils. Intravenous fluids were given, and a Miller–Abbott tube inserted. The patient's condition apparently improved throughout the day. The following night he passed 50 cc. of bright-red blood.

The white-cell count on the seventh hospital day was 22,300, with 91 per cent neutrophils. The urine showed a ++ test for albumin. The nonprotein nitrogen was 44 mg. per 100 cc., the protein 5.8 gm. The chloride was 92.8 milliequiv. per liter, the carbon dioxide combining power 20.6 millimols. The serum amylase was normal. A portable film of the abdomen showed no demonstrable air-filled small intestine. The stomach was filled with air, and the colon contained a large amount of barium and considerable gas.

A film taken on the eighth day showed the tip of the Miller–Abbott tube in the second portion of the duodenum. There appeared to be a small amount of gas in the slightly dilated bowel. A large amount of barium was seen in the large intestine. The right side of the diaphragm was elevated, and there were linear areas of atelectasis in the right lower lung field. The abdomen remained somewhat distended. The Miller–Abbott tube was passed to the jejunum, as confirmed by x-ray, and the stomach was kept decompressed by a Levine tube.

The white-cell count on the eleventh hospital day was 31,300, the hemoglobin 12.6 gm. The blood protein was 6.0 gm. per 100 cc., and the chloride 97.2 milliequiv. per liter. A portable film now showed considerable air in the stomach and some gas-filled bowel, presumably the colon. The Miller–Abbott tube lay over the lumbosacral articulation.

The following day the patient passed dark blood by rectum and had some bloody drainage through the Miller–Abbott tube. He became pulseless, comatose and died.

Differential Diagnosis

Dr. Carroll C. Miller: This case seems to be covered with mystery and confusion concerning several of its details. A large part of the discussion concerns itself with the x-ray findings; none of these prove anything, and so far as I can figure out they do not help particularly in making a diagnosis. There are two points that we must ascertain in diagnosing such a problem: the location of the trouble and whether it is intrinsic or extrinsic in relation to the gastrointestinal tract. If it is intrinsic, is it an infectious condition or is it a vascular disturbance? If it is extrinsic, has it ulcerated into the bowel so as to provide us with an explanation of the symptoms and signs? We should like to know about the presence of abdominal tenderness and pain. The temperature is not recorded. The pulse was essentially normal when the patient first came in, but after the shocklike episode on the sixth day the pulse rose to 120. According to the chart before us, five or six days after admission the temperature rose from the normal to 101°F. by rectum and stayed more or less at that level without any appreciable change. There was a concomitant rise in pulse and respirations. So we do not have a definite picture of a rising curve or of an intermittent spiking one. We do not know what the hemoglobin was when the patient was first seen, so that we have no way of comparing the last note of 12.6 gm. with the former condition.

Since so much space in the abstract has been given to discussion of the x-ray films, it might be interesting to see them now.

Dr. Laurence L. Robbins: These films are arranged more or less according to the time relation in which they were taken. I have left out those that are not particularly pertinent. It might be said that perhaps the diagnosis should have been made by x-ray. I am not at all sure about that, however.

This is the appearance at the time the patient entered the hospital, with a large amount of fecal material on the right side of the colon. The next day, probably after enemas, we notice that the colon is fairly well cleaned out and that there is this air-filled small bowel. The following day a barium enema was given, and the colon is apparently normal. These are the loops of small bowel that

were described as air containing, and you notice that the barium passes up to a point close to the air-filled loops. This loop of ileum appears to go around something (Fig. 1). In the same area you see another loop of ileum that appears to overlie the questionable mass. This loop of bowel is definitely abnormal, I should say. So far as one can tell it is small and probably has some mucosal swelling. I cannot see anything that indicates a definite ulcer. Later films of the small bowel more or less confirm these findings except that there is nothing on which one can make a positive diagnosis of a mass at this time, and the suggestion of the loop of bowel constantly going around something is lost (Fig. 2). In this area, however, the mucosa again appears abnormal and that is confirmed by this spot film. I have seen a similar appearance in the mucosa of the sigmoid in a case of periarteritis nodosa. I am not trying to lead anyone astray, but that is the only similarity I have seen.

FIGURE 1. *X-Ray Film following a Barium Enema.*
The abnormal loop of ileum appears to be partially surrounding a mass over the left side of the lumbosacral junction.

DR. MILLER: How far away from the ileocecal valve would you say this was?

DR. ROBBINS: About 75 cm. An exceptionally large amount of barium passed into the small bowel. I think you can be sure there is definite abnormality of the mucosa of the ileum.

DR. MILLER: Because of the repeatedly high white-cell count and the high percentage of neutrophils, we must assume that something fairly acute in the way of either sepsis or necrosis was going on, and because of a variation during the investigation, at times distention and at times collapse of the bowel, and also because of the terminal episode of hemorrhage into the intestine, we must presuppose that something was going on intraluminally, which allowed blood to escape into the bowel. It will be hard to make a diagnosis that satisfies both these conditions.

There are several things to think of, but we do not have enough evidence to rule them entirely in or out. A sigmoidal diverticulitis with abscess

and rupture might account for localized peritonitis and for subsequent bleeding from the bowel. A mesenteric thrombosis would account for the signs of necrosis in the small intestine, accompanied by hemorrhage coming from a mesenteric thrombosis or an internal hernia with strangulation.

The mass that this loop of bowel encircles might be either abscess or retroperitoneal tumor. It is

FIGURE 2. *X-Ray Film following a Barium Meal.*
The abnormality of the loop of ileum is still visible, but the apparent mass has disappeared.

a high white-cell count and some degree of fever. The chart is possibly consistent with that. It would also account for the terminal bleeding episode. It is not likely that this condition is malignant disease. In the first place, there was no previous history. The man was in reasonably good condition; in fact he was described as being somewhat obese. No masses were felt. However, acute abdominal emergencies are sometimes simulated by extensive metastatic lymph-node involvement in the abdomen because of sudden spread or rupture.

An internal hernia with strangulation of a loop of bowel might account for intermittent obstruction and eventual necrosis of that segment of the bowel, with intraluminal bleeding. I should like to think of the terminal episode as being due to not likely that any retroperitoneal tumor would also so involve the small intestine as to produce this picture. An abscess can involve the wall of the bowel causing obstruction and bleeding, although it is not likely.

A condition that we often forget but which occurs fairly frequently is a Meckel's diverticulitis. In a Meckel's diverticulum there may be bleeding from a peptic ulcer, and it may also become infected, with rupture. From the x-ray picture it is possible that an abscess had formed around a diverticulum of the small intestine and that the loop of bowel had become involved in that area; there might still have been a communication into the lumen of the bowel to account for bleeding by rectum and by the Miller-Abbott tube.

I think we must postulate an infectious process

in the form of an abscess, with involvement of a loop of small bowel. I think as a best bet I shall say that this patient had a Meckel's diverticulum or a diverticulum of the sigmoid — a solitary one that was not seen by x-ray — accompanied by abscess and hemorrhage through erosion of a large mesenteric vessel.

Dr. Robbins: I am not at all sure I made myself clear to you, Dr. Miller. The small-bowel studies do not confirm the presence of the mass suggested by the barium enema; the films are not characteristic of bowel going around a mass.

Dr. Miller: Nevertheless, there is a loop that is abnormal, either by distortion or extrinsic pressure.

Dr. Robbins: It may be intrinsic disease.

Dr. Miller: Of course, a localized regional enteritis is possible, although it is not commonly seen so far back in the ileum as this. Furthermore, I do not believe that in cases of terminal or regional ileitis one often observes a terminal episode such as this patient had, with almost no cachexia or general disturbance.

Dr. Edward B. Benedict: I do not see why this would not go with regional enteritis.

Dr. Robbins: Would one have acute episodes with it?

Dr. Benedict: No.

Dr. Miller: One does not as a rule see such a massive lesion as this man had. Furthermore, such patients are usually younger.

Dr. Richard H. Sweet: As Dr. Miller clearly brought out, I believe there must have been some necrosis of the loop of bowel to explain this picture.

Clinical Diagnoses

Small-bowel obstruction.
Volvulus?
Intussusception?

Dr. Miller's Diagnosis

Meckel's or sigmoidal diverticulitis, accompanied by abscess and hemorrhage.

Anatomical Diagnoses

Mesenteric venous thrombosis.
Infarction of small intestine.
Hemorrhage into intestinal tract.
Peritonitis, acute, fibrinous.
Hemoperitoneum.
Coronary thrombosis, old.
Arteriosclerosis, marked, generalized.

Pathological Discussion

Dr. Benjamin Castleman: At the autopsy we found 3000 cc. of hemorrhagic fibrinous fluid and blood in the abdomen. The entire jejunum and most of the ileum, to within about 150 cm. (6 feet) of the ileocecal valve were covered with bluish fibrin. Parts of the bowel were obviously gangrenous, and other parts showed beginning infarction. The cause of this gangrene was a mesenteric venous thrombosis. The arteries and arterioles were uninvolved. There was no periarteritis nodosa. The entire intestinal tract was filled with old and recent blood, apparently arising from the massive necrosis of the small bowel, which had terminally perforated into the abdominal cavity.

Most of the cases of mesenteric occlusion that we see are arterial in type and are caused by emboli. The venous type is uncommon and little is known about its etiology. In contrast to the arterial it does not usually come on suddenly with severe abdominal pain.

Dr. Robbins: Could you find evidence of old infarction?

Dr. Castleman: The thrombi were of various ages, and in some there was definite organization.

The patient also had an old thrombosis of the left descending coronary artery, which accounted for the anginal attacks.

CASE 29382

Presentation of Case

A fifty-two-year-old man entered the hospital because of severe pain under the xiphoid.

Five years prior to admission the patient suffered his first attack of sharp upper abdominal, midline pain that lasted four or five hours. He entered a community hospital, where extensive studies were done and reported to be negative. He was discharged after two weeks.

Four years and three years prior to admission he had similar attacks of epigastric pain that radiated to both shoulders and to the upper anterior chest. These lasted six and fourteen hours and spontaneously cleared. Seven weeks prior to admission he re-entered the same hospital because of an attack of pain, but since repeated studies were again negative he was promptly discharged. He continued to have these attacks, and six days prior to admission he collapsed during one of them. These episodes had no relation to meals. At times he found that milk and doughnuts partly relieved the pain, and for several years he had drunk 4 to 5 quarts of milk a day. During the previous three months the pain had often been relieved by induced vomiting. There was no nausea, vomiting, anorexia, fever, chills or jaundice. The stools were never tarry, bloody or clay colored. During the previous year constipation had become bothersome but had always been relieved by cathartics.

The patient had lost 15 pounds during the three months prior to admission.

The family and past histories were noncontributory.

Physical examination disclosed a 250-pound man who seemed very restless. The lungs and heart were normal. The abdomen was markedly distended and tympanitic, but peristalsis was normal. No masses were felt, and no tenderness was elicited.

The blood pressure was 110 systolic, 70 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a hemoglobin of 90 per cent, and a white-cell count of 10,200, with 77 per cent neutrophils. The urine was normal. The stool was guaiac negative on two occasions. The blood Hinton test was negative. The nonprotein nitrogen was 14 mg. per 100 cc., the protein 7.5 gm. per 100 cc., and the chloride 99.0 milliequiv. per liter. The van den Bergh reaction was normal.

FIGURE 1. *Portion of Film Showing an Ulcerated Lesion in the Second Portion of the Duodenum.*

A Graham test was negative. A gastrointestinal series disclosed a normal esophagus. The stomach was high and transverse in position but normal in form and function. The duodenal bulb filled to a normal contour. Just beyond the bulb, along the posterior and lateral aspects of the second portion of the duodenum, there was an ulceration 1 by 2 cm. in size. About this area, and extending downward along the second portion of the duodenum for a distance of 7 cm., there was a rigid area of narrowing, and laterally there seemed to be a rather sharply outlined 2-by-4-cm. defect encroaching on the duodenum, in which the ulcer lay (Figs. 1 and 2). Beyond this the duodenum was of rather unusually large caliber. There was no obstruction to the flow of barium through this area. No definite fistulous communications were observed. There were opacities along the course of the colon, probably residue of opaque material previously given.

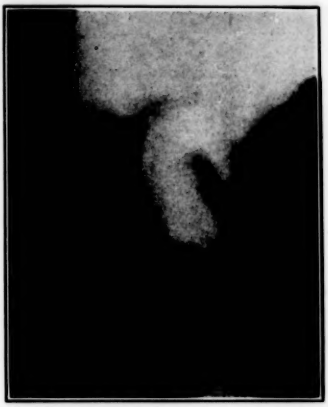

FIGURE 2. *Spot Film Demonstrating the Ulcerated Lesion with Surrounding Edema.*

A barium enema passed readily from the rectum to the cecum and outlined a normal large bowel.

An operation was performed on the thirteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD B. BENEDICT: Practically the only positive finding we have is that seen on the x-ray film. It seems to me that the case is either extremely simple or extremely difficult, and judging from the comments and the strange looks that the people to whom I have talked about it have given me, it looks a little complicated.

The pain radiating to both shoulders seems unusual, so I spoke to Dr. Chester M. Jones about it since he has written a book on digestive-tract pain. He mentioned various possibilities. The heart, from

what I am told, will occasionally give pain radiating to both shoulders, although it is unusual. In this case the heart was entirely normal. Hiatus hernia or other disease of the esophagus with spasm may give pain radiating to both shoulders, but the esophagus was normal by x-ray. Volvulus of the stomach also gives this type of pain, but we have no evidence of that. Gallstones may do it, but the Graham test was negative. The second portion of the duodenum is a rare place for a peptic ulcer, but it may occur.

The fact that there was rigidity of the second portion of the duodenum makes one think of malignant disease in addition to a simple ulcer, but the five-year history is long for malignant disease. It is noted in the x-ray report that the ulcer was situated posteriorly and laterally. Posteriorly the second portion of the duodenum is in relation to the kidney, and it makes one think that possibly this might have been a kidney lesion; but the urine was negative and there were no other signs pointing to a kidney lesion. Laterally the right colic flexure is in relation to the second portion of the duodenum, but the barium enema was negative, which appears to rule out a lesion of the colon that might have perforated into the duodenum. Again, we have the long-standing history that makes a malignant lesion quite unlikely.

Concerning lesions of the pancreas, common bile duct and ampulla of Vater, these organs are all medial, and this lesion was lateral and posterior. Moreover, with a lesion of the pancreas, common bile duct or ampulla, one would naturally expect jaundice. This patient had not been jaundiced. A retroperitoneal lesion other than the kidney, such as sarcoma, might be considered, but the duration seems to have been too long, and I do not believe that I have ever seen one ulcerate into the duodenum.

So we come down to the possibility of simple ulcer of the second portion of the duodenum. These do occur, although they are rare, and everything in the history goes with it. I believe that a peptic ulcer of the duodenum can give pain radiating to both shoulders, which is relieved by milk and doughnuts. He had lost only 15 pounds, which is compatible with a benign peptic ulcer. The physical examination and the laboratory findings contributed nothing. The repeated area of narrowing bothers me, but I think that can go with a cicatricial stenosis associated with a duodenal ulcer. As my first diagnosis, I shall put down benign peptic ulcer of the second portion of the duodenum with cicatricial stenosis, bearing in mind that a carcinoma in that region is also a possibility.

May we now see the x-ray films?

DR. MILFORD SCHULZ: These films of the esophagus and stomach are normal and probably rule out hiatus hernia. The ulcer, which is seen to better advantage on the spot films, lies in this rather constant rounded defect in the second portion of the duodenum.

DR. BENEDICT: Where would you place the ampulla of Vater?

DR. SCHULZ: It should be lower than where the ulcer is, and more medial. This area of narrowing remains quite constant throughout the examination.

DR. BENEDICT: Do you think that it is consistent with a cicatricial stenosis? Or has it got to be a malignant lesion? Or is that not a fair question?

DR. SCHULZ: I should think that either a tumor mass or a scarring of long standing could produce this type of narrowing and constant deformity.

DR. BENEDICT: You are sure it is not medial? It could not be an ulcerating carcinoma of the pancreas?

DR. SCHULZ: No.

DR. BENEDICT: Ulceration of the pancreas is rather unusual on the opposite side of the duodenum. I cannot think of anything else. I shall stick to my original diagnosis.

DR. RICHARD H. SWEET: On a statistical basis would not carcinoma be more frequent than benign ulcer in that location?

DR. BENEDICT: I put that in as a second possibility.

DR. SWEET: I was merely going on the statistical frequency.

DR. BENEDICT: What about the five years' duration?

DR. SWEET: I do not know.

DR. JACOB LERMAN: What about an ulcerating polyp in the duodenum?

DR. SCHULZ: The lesion does not look like a polyp in the x-ray film. It may be a tumor, or it may be just edema of the duodenum.

DR. BENJAMIN CASTLEMAN: The surgeon made leiomyosarcoma of the duodenum as his preoperative diagnosis. Have you anything to say about that?

DR. BENEDICT: I do not believe that I have ever seen one. They are extremely rare.

DR. CASTLEMAN: We have had a few intramural tumors of the second and third portions of the duodenum, but they certainly are not so common as carcinoma or even as peptic ulcer.

DR. FRANCIS D. MOORE: The striking thing about the patient preoperatively was the terrific pain, which was unrelieved by ordinary measures. The diagnosis of leiomyosarcoma was a far-fetched

attempt on the part of the service to reconcile the long history with the existing lesion, with the idea that it might have been a leiomyoma for a period of years and had then undergone malignant degeneration. Dr. Leland S. McKittrick operated on the patient and found a mass in the duodenum that was the size of an orange, a great deal of it apparently being tumor with superimposed inflammatory change. There were no lymph-node or liver metastases. A Whipple operation was performed, the duodenum being removed, the gallbladder anastomosed to the jejunum, a gastrojejunostomy performed and the end of the pancreas closed off. The specimen was opened and showed an ulcerated lesion with raised margins, which appeared to have invaded the surrounding tissue.

Clinical Diagnosis

Leiomyosarcoma of duodenum.

Dr. Benedict's Diagnosis

Peptic ulcer of duodenum.

Anatomical Diagnosis

Peptic ulcer of duodenum.

Pathological Discussion

Dr. Castleman: In the gross we found, 1.5 cm. above the papilla of Vater, a sharply demarcated ulcerated lesion approximately 2.5 cm. in diameter with slightly overhanging edges. As Dr. Moore has said, there was a lot of induration around it, which extended into the surrounding fat. We cut one section through the center of the lesion for microscopic examination and found what looked like a perfectly benign peptic ulcer. Since a peptic ulcer is extremely rare in that location, we went back and made numerous sections of the whole lesion. No evidence of cancer was found, and the final diagnosis was a benign peptic ulcer.

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THE GREAT ARCHITECT

His name is Time. He determines what shall survive, be improved or be developed, and what shall be destroyed, be removed or be relegated to a position of social insignificance. He calls to consult with men on all their projects, and even though he is frequently opposed by individuals, with their wealth and their legacies, his opinion eventually prevails. Man has respect for him, and reverence for the endowments that he has the power to bestow. Man watches his track and measures his passage with the utmost precision, in seconds, minutes, hours, days and years. As the years span into longer periods, arbitrary units are marked off as standards by which men judge their own accomplishments, and with which they vouchsafe the promise of the future.

Tufts College Medical School is now completing such a unit of time; it is fifty years old. Starting as one of many, it has survived to become one of few — there were one hundred and sixty medical schools in this country in 1900, whereas there are but seventy-seven today. Its fifty years have been tumultuous ones in medical education, but from them it emerges an approved school, recognized by all state and national authorities, training one third of the students who enter approved medical schools from the states of Maine, Massachusetts, New Hampshire and Rhode Island, and already backed with a large and vigorous alumni body. Time has firmly established Tufts in the medical life of the country, especially that of New England.

Under other circumstances this fiftieth birthday would be worthy of more pretentious observation than can be accorded it this year. A simple program has been announced, which includes a short series of addresses and a few more intimate occasions, in which there will be participation by students, faculty, graduates and public representatives. A book that permanently records the first fifty years will be issued, and Time will then begin to draw his plans for the second half century.

Having been similarly and generously blessed by the largess of this great architect, the *Journal* extends to Tufts College Medical School hearty congratulations, and best wishes for the years to come.

WARTIME ACTIVITIES ARE DIFFERENT

THE Directing Board of the Procurement and Assignment Service, War Manpower Commission, in its release reprinted elsewhere in this issue of the *Journal*, calls attention to the critical shortage of nurses for wartime needs and to changes in our practices necessitated thereby. As with many other groups it is manifestly impossible to train sufficient nurses soon enough to meet the needs we are about to face. The present likelihood

that we shall be spared the bombing meted out to so many other parts of the world (yet justifiably feared by us a year ago) should not permit anyone to imagine that the national crisis has yet been reached — let alone passed.

The circumstance that so many people have so much more money than they have ever had before, with so much less to spend it on, has operated to produce an increase in demand for medical and nursing services. The only deterrents are the distinctly limited number of physicians and nurses available to supply these services, and the effect of public opinion on those tempted to indulge themselves unnecessarily in the luxuries of being ill. Both these deterrents are effective, but they can and should be made still more effective if the Nation is to muster its full potential effort. The disappearance in Great Britain of all forms of civilian psychoneurosis indicates the degree to which any population may aspire in restricting itself to bare essentials.

The statement that more changes must be planned and executed to place nursing on a wartime basis seems to be an inevitable truth. The American Red Cross has accepted the responsibility of recruiting 36,000 nurses during the coming year, and certain important duties have been assigned to the recently organized Nursing Division of the Procurement and Assignment Service. That pressure may be brought to bear by the War Manpower Commission has been amply demonstrated in other fields, and the Procurement and Assignment Service will undoubtedly reach a point at which its opinion of availability or essentiality for certain nurses will not agree with that of the nurses themselves. When this point is reached, other measures must be devised. These will be more difficult in the case of women than the various ways that have been suggested to coerce men under comparable conditions. When coercion needs to be invoked, however, the method is immaterial: the country has begun to scrape the bottom of its barrel, and there is never much of value to be found among the dregs.

All the changes being brought into field after field by this war are not going to be temporary; they may endure beyond the duration. The thought that "the service of two part-time nurses can equal that of one full-time one" has a corollary, namely, that one full-time nurse can cover the jobs of two part-time ones. It is going to be as painful to decelerate as it has been to accelerate our activities — and there will undoubtedly be some that will remain accelerated. What this war is doing, primarily, is breaking down traditions — both good and bad. The good can be restored; the bad had better remain broken. In the meantime, he who resists the changes of today must prove to the rest of the world that he is not old and decrepit.

MEDICAL EPONYM

Gee-Herter's Disease

This was described by Samuel Gee (1839–1911), physician to Saint Bartholomew's Hospital, London, in his paper "On the Coeliac Affection," which appears in *Saint Bartholomew's Hospital Reports* (**24**: 17–23, 1888). A portion of the article follows:

> There is a kind of chronic indigestion which is met with in persons of all ages, yet is especially apt to affect children between one and five years old. Signs of the disease are yielded by the faeces; being loose, not formed, but not watery; more bulky than the food taken would seem to account for; pale in colour, as if devoid of bile; yeasty, frothy, an appearance probably due to fermentation; stinking, stench often very great, the food having undergone putrefaction rather than concoction. . . .
>
> To diarrhoea alba add emaciation and cachexia, and we have a complete picture of the disease.

Twenty years later, Christian Archibald Herter (1865–1910), professor of pharmacology and therapeutics at Columbia University, wrote a book entitled *On Infantilism from Chronic Intestinal Infection* (New York, 1908). The following summary is found on page 113:

> 1. There is a pathological state of childhood marked by a striking retardation in growth of the skeleton, the muscles and the various organs and associated with a chronic intestinal infection characterized by the overgrowth and persistence of bacterial flora belonging normally to the nursling period. To this condition may be applied the term "intestinal infantilism."

2. The chief manifestations of intestinal infantilism are arrest in the development of the body; maintenance of good mental powers and a fair development of the brain; marked abdominal distension; a slight or moderate or considerable degree of simple anaemia; the rapid onset of physical and mental fatigue; irregularities of intestinal digestion resulting in frequent diarrhoeal seizures. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

STETSON — HALBERT G. STETSON, M.D., of Greenfield, died September 15. He was in his seventy-sixth year.

Dr. Stetson received his degree from the College of Physicians and Surgeons of Baltimore in 1895. Since 1921, he had served as medical examiner, and he was also chairman of the Greenfield school board and president of the Franklin County Public Hospital Corporation. Dr. Stetson was a former president of the Franklin County Medical Society, the New York and New England Association of Railway Surgeons, the Connecticut Valley Medical Association and the Massachusetts Medical Society. He was a fellow of the American Medical Association.

WYLIE — EUGENE C. WYLIE, M.D., of Dorchester, died September 15. He was in his seventy-second year.

Dr. Wylie received his degree from Harvard Medical School in 1895. He had been a practicing physician in Dorchester for over forty-eight years and a member of the staff of the Children's Hospital for twenty years. He was a member of the Massachusetts Medical Society and the American Medical Association.

A brother survives.

WAR ACTIVITIES

PROCUREMENT AND ASSIGNMENT SERVICE

Under the caption "Wartime Nursing Is Different," the Directing Board of the Procurement and Assignment Service, War Manpower Commission, has recently released the following statement.

It is utterly impossible to provide the necessary volume of wartime nursing service on a peacetime basis. Places where nursing is going on as usual must share with others. Nurses who have not made adjustments to wartime needs for their service should understand the necessity for their participation.

The National Nursing Council has pointed out that the value of any national plan must be judged by its usefulness at the local level, that is, where nurses live and work — in the country and in the villages, towns and cities of the Nation.

Wartime nursing is different! That inescapable fact must be generally accepted by nurses, by physicians and by hospital administrators. Energy and motion now spent in resistance to change must be released for the attack on war-created needs.

Nurses have wrought many changes, but not enough, in the pattern of nursing service since Pearl Harbor. "We just do the best we can" is heard more frequently than "This is our plan." Generally speaking, educational programs have received more thought than service programs. Acceleration of the basic course in nursing is an outstanding example. State boards of nurse examiners have initiated others.

The principles of good nursing have not changed, but nurses are learning to concentrate on the essentials. In the analysis and administration of nursing service, radical changes are being made. Tremendously valuable assistance in caring for patients is being secured from the Red Cross nurse's aides and other volunteers as well as from paid auxiliary workers.

Thus far nursing service has not been rationed; such rationing would be complicated by the differences in individual nurses and by the degree of essentiality of needed services. Furthermore, the sharing of services is more difficult than the sharing of goods. A critical shortage of nurses exists. Over 36,000 nurses are now with the armed forces and the Red Cross has accepted responsibility for the recruitment of an equal number by June 30, 1944. Our men are receiving skilled medical care of a high order, as shown by the high percentage of recovery from injury. Skilled nursing is an important factor in such care. Then, too, the very presence of nurses near the bases of military operations has repeatedly been described as a potent force in maintaining morale.

There has been an unprecedented increase in the use of civilian hospitals. Hospitals gave 14,250,000 more days of care in 1942 than in the preceding year, and the trend still is definitely upward. This is in keeping with the rapid growth of Blue Cross (group-hospitalization) plans and the Children's Bureau hospitalization program for the care of the families of service men.

Nursing is essential to the nation's health. The national nursing inventories of nursing resources in 1941 and 1943, made by the United States Public Health Service, offer a comparison of data for the two years (Table 1).

TABLE 1. *National Nursing Inventories.*

CLASSIFICATION	1941	1943
Active:		
Institutional	81,708	77,704
Public health	17,766	18,900
Industrial	5,512	11,220
Private duty	46,793	44,299
Other	21,276	18,476
Inactive but available	25,252	38,746*
Inactive and not available	90,979	49,829
Totals	289,286	259,174
In Nurse Corps of Army and Navy	6,371	36,000†

*Of these, 23,576 are married and under forty.

†Precise data are not available.

The total number of nurses graduated in the intervening two years is well in excess of the number withdrawn for military service; this fact is not apparent in the inventory. The returns are apparently incomplete. Active nurses who did not return their questionnaires apparently did not realize the profound importance of the information requested. This information is the basis for present planning and safeguarding the future. The relatively small decrease in the number of institutional nurses is much less significant than the increased use of hospitals in

creating the serious shortage of nurses. The increased number of nurses in industrial nursing is, of course, not surprising.

The large number of inactive nurses who reported themselves available is encouraging. But, — they are available for what, — full time or part time? These nurses and others who are still "hidden" can make a valuable contribution to nursing resources. Although it requires a little more planning, the service of two part-time nurses can equal that of one full-time one. Wartime nursing puts a tremendous burden on all the administrative nurses.

The program of the recently organized Nursing Division of the Procurement and Assignment Service is as follows: to determine the availability for military service or the essentiality for civilian service of all nurses eligible for military service and to submit such determinations to the American Red Cross for use in the procurement of nurses for the armed forces; to promote plans for maximum utilization of fulltime nurses and those who are able to serve only part time; to develop and maintain a roster of all graduate registered nurses; and to develop and encourage sound methods of supplementing the work of nurses with nonprofessional personnel.

Through the War Manpower Commission, nursing will not only have the benefit of the experience in the procurement and assignment of physicians, but means will be found to interpret wartime nursing to physicians and to secure their co-operation in effecting desirable wartime adjustments.

CORRESPONDENCE

BOARD OF REGISTRATION IN MEDICINE

To the Editor: At a meeting of the Board of Registration in Medicine held on July 16, 1943, Dr. H. Quimby Gallupe, of Waltham, was re-elected secretary of the Board and Dr. Edward A. Knowlton, of Holyoke, was elected chairman.

Governor Saltonstall recently appointed Dr. George L. Schadt, of Springfield, as a member of the Board to fill the expired term of Dr. Harry L. Stevens, of New Bedford, and Dr. William F. O'Reilly, of Lynn, as a member to fill the unexpired term of Dr. Francis R. Mahony, of Lowell, deceased.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

ASPIRATION OF PLEURAL EFFUSIONS AND OF HEMOTHORAX WITH AIR REPLACEMENT

To the Editor: An article in the June 12 issue of the *Journal of the American Medical Association* reflected a dependence in our armed forces on the Potain aspirator, and a device was described for aspiration by means of a piston syringe. Apparently forgotten, however, is the time-tested and satisfactory use of a simple syphon tube by which the fluid is made to flow from the chest to a basin on the floor by force of gravity alone.

All that is necessary is an aspirating needle attached to a rubber tube and a clamp or plug to occlude the distal end. The needle and tube are then filled with water and the tube stopped before sterilizing. After sterilizing, the stopped end of the water-filled tube is allowed to rest in a basin on the floor by the bedside; the needle is inserted in the chest; then the clamp or plug is removed and the chest-fluid flows down into the basin.

This method was devised by Dr. W. W. Gannett at the Massachusetts General Hospital and was in constant use on his service during my internship in 1902. It has been employed by me, and presumably by many others, ever since in preference to the clumsy and unreliable Potain aspirator.

If one prefers, the process may be started by drawing on a piston syringe attached to the distal end of the tube. This has the advantage of yielding specimens undiluted with water. But when the tube is filled and siphonage established it is much better to allow the flow to continue steadily and gently by gravity alone rather than by intermittent manipulation of the syringe.

It is commonly recognized that in the hemothorax of through-and-through gunshot wounds it is inadvisable to apply simple aspiration with re-expansion of the wounded lung. On the other hand, there is probable advantage in removing the accumulation of defibrinated blood, provided this can be done without expanding the lung. Thus, aspiration with simultaneous creation of artificial pneumothorax is practiced. The following method, which I devised while on duty with the Harvard Unit at General Hospital No. 22, B.E.F., in 1916, was found to be practical and was used extensively at that hospital.

The principle involved is that if a closed, air-containing bottle on the floor is connected with the fluid-containing pleural cavity by two tubes and needles, and if a flow by siphonage from chest to bottle is started in one of these tubes, an automatically equal amount of air will be transferred from the bottle to the chest through the other tube. Thus the fluid in the chest will be replaced by air, but throughout the process the intrathoracic pressure will remain constant.

All that is necessary is a glass bottle of 2-quart size or larger, a two-hole rubber stopper with glass tubes, fitting without air-leaks, and two rubber tubes 3 to 4 feet long with an aspirating needle at one end of each, the other ends connecting with the glass tubes of the bottle. The whole assembly is sterilized together.

Some means of starting the siphonage must be provided. The simplest way is to fill one of the tubes with water and to clamp it near the bottle end before sterilizing. An alternative is to insert a three-way stopcock or T tube and aspirating syringe in the course of the tube through which the outflow is to be started.

For use, the assembled and sterilized apparatus is placed at the bedside. Two points on the chest are marked and infiltrated with novocain — one rather low, and the other about two spaces higher. If any uncertainty concerning the correctness of their location exists, it is well to prove the productiveness of both by puncture with an ordinary syringe and needle. Then the needle of the tube through which outflow is to be established is inserted in the chest at the lower point, the bottle is lowered to the floor and the flow is started. If the water-filled tube method has been employed, one merely releases the clamp after lowering the bottle, and siphonage by the water in the tube will initiate a continuous flow from the chest to the bottle. If aspiration by syringe is applied, the tube is pinched or clamped below the T tube and fluid is drawn into the syringe; then, the tube being released, ex-

pulsion of fluid from the syringe will start the siphonage, which continues by force of gravity. The fluid of hemothorax is so thoroughly defibrinated that the flow is rarely interrupted.

Commonly, in practice, the heart is markedly displaced, so that it may be well to defer insertion of the second needle until this displacement has been somewhat reduced. Soon, however, the air replacement is started by inserting the second needle at the higher puncture-point. By listening with a stethoscope, one can hear the bubbles of entering air, which proves that the system is operating satisfactorily. In due course the physical signs of hydropneumothorax appear — tympany above a horizontal level of flatness. The cough of pulmonary edema, which is the usual signal for terminating simple aspirations, seldom occurs, so that usually the flow may be allowed to continue until it ceases.

Both these procedures operate by means of the negative pressure induced by a column of fluid equal in height to the distance between the chest and the floor. Variations in intrathoracic pressure, as measured by a water manometer, are surprisingly slight so that this degree of aspirating force is adequate to maintain a constant flow, since it exceeds by a wide margin any negative pressure that may occur in the chest. Moreover, the steady, gentle flow by siphonage is far less apt to cause disagreeable reactions than is the irregular, more forcible aspiration by other methods. In my opinion, aspiration by siphonage deserves general adoption, not only under primitive conditions for its simplicity but also in the best hospital practice for its other advantages.

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BOOK REVIEWS

From Witchcraft to Chemotherapy. By Sir Walter Langdon-Brown, M.D., D.Sc. (hon.), F.R.C.P. The Linacre Lecture, 1941. 12°, paper, 60 pp. Cambridge, England: Cambridge University Press, 1941. 60c.

This is a brief but thoroughly interesting story of the increasing means of healing employed in medicine from early witchcraft to the latest triumph of chemotherapy. Dr. Brown shows that the homeopathic dictum that like cures like may be traced to the sympathetic form of magic and that the forerunner of plasters and poultices was a form of contagious magic. He further points out that the old wives' tales concerning magical cures are based on witchcraft, which in turn arose from the fertility cults of organized religion. Herbal remedies were in use because chemistry had not advanced sufficiently to form any basis for rational therapeutics. Only gradually did therapeutics evolve to its present triumphant position. College libraries should find this small book a valuable addition to their shelves.

A Study of the Blood in Cancer, with Special Reference to the Needs of the Tumor Clinic. By O. Cameron Gruner, M.D. (Lond.). 4°, cloth, 100 pp., with 40 illustrations, 4 plates and 32 tables. Montreal: Renouf Publishing Company, 1942. $4.00.

This is an odd book. It has evidently been written by a man with so passionate an interest in the diagnosis of cancer that he will sit for long hours in the laboratory studying the many minute characteristics of blood films — fresh, stained, dark-field and so forth. Unfortunately this laudable enthusiasm has probably far outstripped the importance of these hematologic minutiae in the diagnosis and prognosis of cancer.

The author states that by studying the following features of the blood, one may arrive at a tentative diagnosis of cancer and its degree of severity: viscosity (*v*), that is, case of spread of the blood smear; crenation of red cells (*c*); fibrin formation (*f*); granular matter (*g*); ameboid movement of the leukocytes (*a*); leukocytosis (*l*); pattern formed by the red cells (*t*); agglutinating tendency of red cells (*ag*); rouleaux formation (*ro*); autohemolysis (*h*); size of the red cells (*s*). The matter of intracellular granules is also discussed. These features are then qualified by degrees, and one may then arrive at a formula such as the following, which is stated to be an example of cancer:

$$v^3\, c^3\, f^3\, g^3\, a^3\, l^1 - t^3\, (ag^3\, ro^6)\, h^3\, s^3$$

That all the above abnormalities may occur in various other conditions, that they are extremely variable and that they depend in large part on technic, cleanliness of glassware and so forth is not overemphasized.

The actual relation of these widely dissimilar features to cancer is by no means proved either statistically or clinically. To confirm or disprove the author's contentions would require years of study and careful statistical analysis. One doubts that it is worth the effort.

Infant and Child in the Culture of Today: The guidance of development in home and nursery school. By Arnold Gesell, M.D., and Francis L. Ilg, M.D. In collaboration with Janet Learned, M.A., and Louise B. Ames, Ph.D. 4°, cloth, 399 pp. New York and London: Harper and Brothers, 1943. $4.00.

Dr. Arnold Gesell is director of the Yale Clinic of Child Development and has made notable contributions in this field since the clinic was established in 1911. Furthermore, it has become the habit of those working with children to turn to Dr. Gesell's publications constantly for authoritative information about the mental growth of infants and young children. In his latest publication the author has brought together in compact form much of the experience based on the research conducted at the clinic.

The book is divided into three parts. The first is concerned primarily with the broader aspects of the relation of growth to environmental and cultural factors. The second is a detailed description of the growing child. The third is a discussion of growth guidance, and includes much wise counsel in the training of children.

Dr. Gesell portrays throughout this book his sound philosophy concerning children and their relation to the world in which they must live. The book should be of immense value to physicians, to teachers and to anyone interested in children. One rarely finds so much sound scientific information combined with practical guidance as in this book. It can be unreservedly recommended.

Victories of Army Medicine: Scientific accomplishments of the Medical Department of the United States Army. By Edgar E. Hume, M.D., D.P.H., D.T.M. and LL.D. 8°, cloth, 250 pp., with 79 illustrations. Philadelphia: J. B. Lippincott Company, 1943. $3.00.

Colonel Hume is well known for his many contributions on the history of the Medical Department of the United States Army. This book is based on lectures given before the College of Physicians of Philadelphia and Johns Hopkins University and on the Beaumont Lecture before the Wayne County Medical Society, Detroit. The volume covers the complete record of the Medical Department and the Medical Museum of the United States Army.

Beginning in 1775, with the War for Independence, and extending through World War II up to the present time, details are given in regard to the history of army medicine. Subsequent chapters deal with the *Index Catalogue* of the Army Medical Library, the Medical Museum and the School of Preventive Medicine. Colonel Hume has added, moreover, an analysis of the contributions of the Army to surgery, physiology and epidemiology and to the discovery of various diseases. Naturally, emphasis is put on the work of Walter Reed and William Beaumont, but Colonel Hume has dug out from the records numerous other contributions by various men connected with the service who perhaps are not so well known.

The book is well written, and there are numerous excellent illustrations. Title pages of important books are given, as well as photographs of men grouped into certain categories, such as medical bibliographers, pioneers in photomicrography, vital statisticians, ornithologists and meteorologists. An excellent account is given of Colonel John Shaw Billings, one of the greatest of military surgeons. The appendix carries tables, giving a list of the directors of the Medical Department of the United States Army from 1775, of librarians of the Army Medical Library, of curators of the Army Medical Museum and of others. There is also a list of general hospitals, each being named for a physician who served the Medical Department. The place and time of his service and the nature of the work that he did are indicated.

In general, this is an excellent book, covering the field as it has never been covered. Although there have been histories of the Medical Department of the United States Army, particularly the one published in 1929 by Colonel Ashburn, Colonel Hume has written a different type of book — an illustrated history in a semipopular manner, based on sound facts. The book should appeal not only to the medical profession but also to the general public.

Manual of Industrial Hygiene and Medical Service in War Industries. Issued under the auspices of the Committee on Industrial Medicine, Division of Medical Sciences, National Research Council. Prepared by the Division of Industrial Hygiene, National Institute of Health, United States Public Health Service, and edited by William M. Gafafer, D.Sc. 8°, cloth, 508 pp., with 20 illustrations and 5 tables. Philadelphia and London: W. B. Saunders Company, 1943. $3.00.

This manual has been prepared by the Division of Industrial Hygiene, National Institute of Health, of the United States Public Health Service, and presents a comprehensive discussion of industrial-health problems involving organization, operation, the prevention and control of disease and the problems associated with manpower shortages. Sixteen well-qualified specialists in various fields of industrial medicine and public health have contributed to the volume, which is a desirable handbook for all engaged in caring for large groups of workers.

A Surgeon's Fight to Rebuild Men: An autobiography. By Fred H. Albee, M.D. With a foreword by Lowell Thomas. 8°, cloth, 349 pp., with 10 illustrations and a frontispiece. New York: E. P. Dutton and Company, Incorporated, 1943. $3.50.

This is an interesting autobiography by a man who has played a distinct part in the development of orthopedic surgery in this country. He is well known for his contributions to bone-graft surgery and the development of numerous mechanical devices that have made operations on bones easier and more efficient. His life, moreover, has had a certain dramatic quality, particularly in his early days; for Dr. Albee has not been without criticism from his colleagues, while at the same time receiving honors both from scientific bodies and from the public.

The author was born in 1876 near Wiscasset, Maine, of English and French Huguenot stock. From his grandfather Houdlette, who was an expert cabinetmaker, young Albee learned much about mechanical problems and the use of his hands in delicate work. Such problems interested him all his life, and it is not surprising that he became a highly skilled manipulator of orthopedic apparatus with a finely developed sense of surgical technic. He earned his way through Bowdoin College and later attended Harvard Medical School. While there he had intimate contacts with some of the professors and writes about Richard Cabot, J. J. Putnam, R. H. Fitz, A. T. Cabot and M. H. Richardson. Under Dr. Cabot's direction he worked for Dr. Putnam in the old Colby Hydrotherapy Institute, taking blood pressures on patients who were being treated. Dr. Richardson kept an eye on this "young, green lad from the East," to use Albee's own expression, and made him prosector, with John Homans, in preparation for Dr. Richardson's lectures.

After leaving the Massachusetts General Hospital, he began practice in Waterbury, Connecticut. While there he went to New York City every week to attend orthopedic clinics, particularly at the Hospital for the Ruptured and Crippled and the New York Postgraduate Hospital. He soon became well known, even abroad, and while still in Waterbury, in 1906, he fused the hip joint of a patient by a bone-graft. This new method of arthrodesis brought him into the limelight and he was invited to go to Budapest in 1909, while still a very young man, to demonstrate his operation. There he was received with acclaim.

After coming home, he worked hard on orthopedic surgery, particularly at the animal laboratory in Cornell Medical School, where he was soon made professor of orthopedic surgery. In 1911 he first used living bone as a bone-graft in the treatment of Pott's disease, basing his operation on two sound principles that have largely been widely accepted; in the first place, Albee stated that the graft must be so fitted that a sound blood supply is as-

sured, and secondly, that the graft must come from the same species.

The rest of Albee's life is possibly of less medical interest although more important, perhaps, to the public. He served in the Army during World War I and afterward. In addition he took an active part in the development of orthopedic surgery, not only in this country but abroad, and helped to establish international orthopedic congresses in collaboration with his foreign colleagues. In 1929, when he was president of the American Orthopaedic Association, he arranged a joint meeting with the British Orthopaedic Association in London. Subsequently Dr. Albee established a private clinic in Florida.

The book is fairly well written, but there are a number of minor typographical errors. The illustrations are in general excellent and facts of considerable historical importance are contained in this volume, particularly in the early chapters.

Brucellosis in Man and Animals. By I. Forest Huddleson, D.V.M., Ph.D. Revised edition. 8°, cloth, 379 pp., with 42 illustrations and 36 tables. New York: The Commonwealth Fund, 1943. $3.50.

The first edition of this excellent monograph, issued in 1934, carried on the frontispiece the following prediction made by Alice C. Evans in 1918, when she discovered that *Brucella melitensis*, the causative agent of undulant fever, and Bang–Striholt's bacillus, which produced epizootic abortion in cattle, showed a hitherto unsuspected kinship: "Considering the close relationship between the two organisms, and the reported frequency of virulent strains of *Bact. abortus* in cows' milk, it would seem remarkable that we do not have a disease resembling Malta fever prevalent in this country." These words have been replaced by the equally divinatory ones of Charles Nicolle: "Mediterranean [undulant] fever is a disease of the future."

Keeping the same title Dr. Huddleson's primitive compilation of methods for the diagnosis and study of brucellosis has grown up to a treatise giving, besides detailed technical information, a complete presentation of the historical developments and of the data gathered in recent years concerning the nature, treatment and control of the disease. The book relates that in the United States the reported cases of brucellosis in man have steadily increased from 24 in 1925 to 3427 in 1941. The prophecies quoted above are on their way to realization, since Dr. D. W. Giltner warns that brucellosis in cattle has become already three times as prevalent as was tuberculosis at the time its eradication began.

This edition ought to be read by all public-health officers, since the section dealing with sanitary problems is written by Dr. Giltner, whose qualification in this field is unmatched. Other important improvements have been introduced and recent contributions not heretofore published have been included.

The 1939 edition paved the way from the booklet issued in 1934 to the 1943 monographic presentation, which by no means contains all the information available, since many data and investigations related to immunity have not been included. In this connection, attention is called to a review on immunity that appeared in the June, 1942, issue of *Bacteriological Reviews*. A melting of both sources of information would provide a valuable body of references. The bibliography, though yet incomplete, already embraces 500 titles. The 1943 revision is not considered by Huddleson himself as the *dernier mot* on the matter treated; however, the untiring efforts of a man who has been studying a disease for more than a quarter of a century deserve the keen interest of and a warm welcome from the research as well as the professional worker.

Synopsis of Pathology. By W. A. D. Anderson, M.D. 12°, cloth, 661 pp., with 294 illustrations and 17 color plates. St. Louis: The C. V. Mosby Company, 1942. $6.00.

This synopsis of pathology concentrates in a brief survey a tremendous number of facts. It shows that the author is able to differentiate essentials and nonessentials, and the restricted bibliographic references at the end of each chapter are well chosen. By means of frequent tables, he makes an excellent synoptic presentation, particularly in the fields of hematology and lymphatic diseases. The chapter on parasites, however, needs some amplification since no mention is made of Bilharzia and cysticercosis.

The illustrations are in general well chosen and well reproduced, but one would prefer for the demonstration of tuberculosis to students a spleen with smaller tubercles than the one which has been chosen and which so closely resembles the illustration of the spleen in Hodgkin's disease. For the purpose of ordinary demonstration miliary tuberculosis, which is manifest with three to five magnifications, is perhaps the best.

The opinion of the reviewer approaches somewhat that of the old gambler: "Don't gamble, but if you do, take the bank." Thus, the best advice seems to be to use a standard textbook in pathology. A good synopsis, such as that of Anderson, may satisfy the student and prevent his going to the more complete sources of information.

Man in Structure and Function. By Fritz Kahn, M.D. Translated from the German and edited by George Rosen, M.D. 2 vol. 8°, cloth, Vol. 1, 341 pp., with 207 illustrations, and Vol. 2, 397 pp., with 253 illustrations. New York: Alfred A. Knopf, 1943. $10.00 (set).

This is a popular account of the anatomy and physiology of man, illustrated by a series of remarkable pictures. Based on sound scholarship, a thorough knowledge of physiology and a style suitable for the general public, nothing of its kind has ever before been written. In the reviewer's opinion, the book is by far the best of its type. The pictures are perhaps the most remarkable part of it, and any physician in looking them over is sure to gain knowledge of some of the complex physiologic processes of the body not directly in his special field of activity.

For the public these volumes are indeed a welcome addition to the literature. The book was first published in Switzerland in 1939, and it is greatly to the credit of the publisher that he had the foresight to issue this elaborate two-volume work at the present time. A sound knowledge of the body was never more needed by the American public than now, when the problems of nutrition are in the forefront. The translation from the German is excellent, and the price of the volumes is entirely justified by the contents.